



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 106248

TO: Rebecca Cook  
Location: CM1/2B07/2D01  
Art Unit: 1614  
Wednesday, October 22, 2003  
  
Case Serial Number: 09/843132

From: Barb O'Bryen  
Location: Biotech-Chem Library  
CM1-6A05  
Phone: 308-4291 *BOB*  
  
barbara.obryen@uspto.gov

### Search Notes



Baib O'Brien

Access DB# 106248

# SEARCH REQUEST FORM

Scientific and Technical Information Center

OCT 23 21

Requester's Full Name: Rebecca Losh Examiner #: \_\_\_\_\_ Date: 10/20/03  
Art Unit: 1614 Phone Number 308 4724 Serial Number: 09/843132  
Mail Box and Bldg/Room Location: CUY Results Format Preferred (circle): PAPER DISK E-MAIL  
DB01

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_


Inventors (please provide full names): John McKean

Earliest Priority Filing Date: 12/23/98

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

1. Please provide structures for <sup>a</sup>irinotecan & <sup>b</sup>celecoxib
2. What is definition for 'neoplasia'
3. search a <sup>(3A)</sup> & b to treat neoplasia. What <sup>(3B)</sup> would rationale be to use COX-2 inhibitor (b) with DNA topoisomerase I inhibitor (a)

Thanks  
Rebecca

 Search Approval

TK Page  
SPE, AV 10/16

## STAFF USE ONLY

Searcher: PROB Type of Search \_\_\_\_\_ Vendors and cost where applicable  
NA Sequence (#) \_\_\_\_\_ STN: 123  
Searcher Phone # \_\_\_\_\_ AA Sequence (#) \_\_\_\_\_ Dialog \_\_\_\_\_





# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact:*

Mary Hale, Information Branch Supervisor  
308-4258, CM1-1E01

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 - Circ. Desk





## Stedman's Medical Dictionary 27th Edition

### neoplasia (ne-o-pla'ze-a)

The pathologic process that results in the formation and growth of a neoplasm. [neo- + G. *plasis*, 1 a molding] **cervical intraepithelial neoplasia** dysplastic changes beginning at the squamocolumnar junction in the uterine cervix that may be precursors of squamous cell carcinoma: grade 1, mild dysplasia involving the lower one-third or less of the epithelial thickness; grade 2, moderate dysplasia with one-third to two-thirds involvement; grade 3, severe dysplasia or carcinoma in situ, with two-thirds to full-thickness involvement. **lobular neoplasia** SYN: noninfiltrating lobular *carcinoma*. **multiple endocrine n. (MEN)** a group of disorders characterized by functioning tumors in more than one endocrine gland. SYN: familial multiple endocrine *adenomatosis*, multiple endocrine *adenomatosis*. **multiple endocrine n. 1 [MIM\*131100]** syndrome characterized by tumors of the pituitary gland, pancreatic islet cells, and parathyroid glands and may be associated with Zollinger-Ellison syndrome; autosomal dominant inheritance, caused by mutation in the MEN1 gene on chromosome 11q. **multiple endocrine n. 2 [MIM\*171400]** syndrome associated with pheochromocytoma, parathyroid adenoma and medullary thyroid carcinoma; autosomal dominant inheritance, caused by mutation in the RET oncogene on chromosome 10q. **multiple endocrine n. 3 [MIM\*162300]** syndrome characterized by tumors found in MEN2, tall, thin habitus, prominent lips, and neuromas of the tongue and eyelids; autosomal dominant inheritance, caused by mutation in the RET oncogene on 10q. SYN: multiple endocrine *n. 2B*. **multiple endocrine n. 2B** SYN: multiple endocrine *n. 3*. **multiple endocrine n., type 1** SYN: multiple endocrine neoplasia *syndrome*, type 1. **multiple endocrine neoplasia, type 2A (MEN2A)** SYN: multiple endocrine neoplasia *syndrome*, type 2A. **prostatic intraepithelial neoplasia (PIN)** dysplastic changes involving glands and ducts of the prostate that may be a precursor of adenocarcinoma; low grade (PIN1 1), mild dysplasia with cell crowding, variation in nuclear size and shape, and irregular cell spacing; high grade (PIN1 2 and 3), moderate to severe dysplasia with cell crowding, nucleomegaly and nucleolomegaly, and irregular cell spacing. **vaginal intraepithelial n.** preinvasive squamous cell carcinoma (carcinoma in situ) limited to vaginal epithelium; like vulvar or cervical intraepithelial neoplasia, graded histologically on a scale from 1 to 3 or subdivided into low-grade and high-grade intraepithelial malignancy; usually related to human papilloma virus infection; may progress to invasive carcinoma. **vulvar intraepithelial n.** preinvasive squamous cell carcinoma (carcinoma in situ) limited to vulvar epithelium; like vaginal or cervical intraepithelial neoplasia, graded histologically on a scale from 1 to 3 or subdivided into low-grade and high-grade intraepithelial malignancy; usually related to human papilloma virus infection; may progress to invasive carcinoma.

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## Stedman's Medical Dictionary 27th Edition

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### neoplasm (ne'o-plazm)

An abnormal tissue that grows by cellular proliferation more rapidly than normal and continues to grow after the stimuli that initiated the new growth cease. Neoplasms show partial or complete lack of structural organization and functional coordination with the normal tissue, and usually form a distinct mass of tissue that may be either benign (*benign tumor*) or malignant (cancer). SYN: new *growth*, tumor (2). [neo- + G. *plasma*, 1 thing formed]  
**histoid n.** old term for a *n.* characterized by a cytohistologic pattern that closely resembles the tissue from which the neoplastic cells are derived.

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Thomson PDR. All rights reserved.



=> fil reg; d ide 11 1-2; d ide 12

FILE 'REGISTRY' ENTERED AT 09:14:12 ON 22 OCT 2003  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 21 OCT 2003 HIGHEST RN 607679-40-3  
DICTIONARY FILE UPDATES: 21 OCT 2003 HIGHEST RN 607679-40-3

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS on STN

RN 100286-90-6 REGISTRY

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-  
tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-  
b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline, [1,4'-bipiperidine]-1'-  
carboxylic acid deriv.

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-  
4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl  
ester, monohydrochloride, (S)-

OTHER NAMES:

CN 7-Ethyl-10-[[4-(1-piperidyl)-1-piperidyl]carbonyloxy]camptothecin  
hydrochloride

CN Campto

CN Camptothecin 11

CN Camptothecin 11 hydrochloride

CN CPT 11

CN Irinotecan hydrochloride

CN Topotecin

CN U 101440E

FS STEREOSEARCH

DR 111348-33-5

MF C33 H38 N4 O6 . Cl H

SR CA

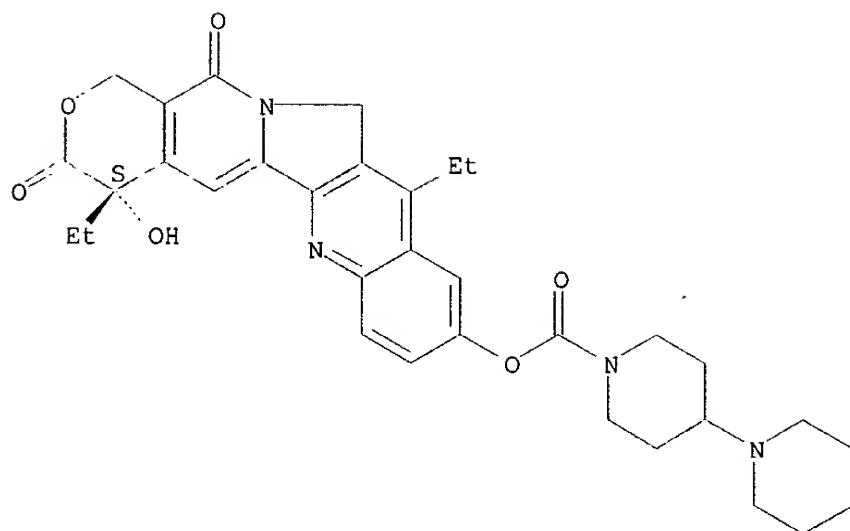
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU,  
DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK\*,  
PHAR, PHARMASEARCH, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USPAT2,  
USPATFULL

(\*File contains numerically searchable property data)

CRN (97682-44-5)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

522 REFERENCES IN FILE CA (1907 TO DATE)

7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

527 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS on STN

RN 97682-44-5 REGISTRY

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline, [1,4'-bipiperidine]-1'-carboxylic acid deriv.

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, (S)-

OTHER NAMES:

CN (+)-Irinotecan

CN Camptosar

CN **Irinotecan**

FS STEREOSEARCH

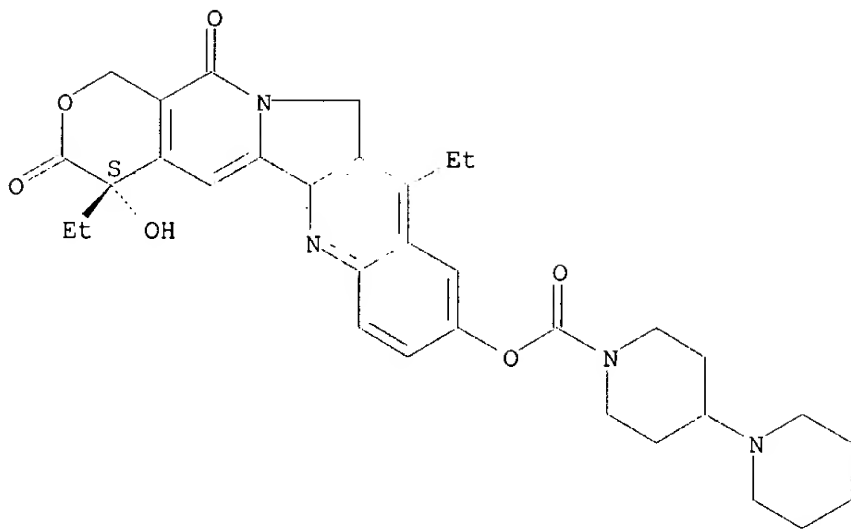
MF C33 H38 N4 O6

CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, IPA, MRCK\*, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

719 REFERENCES IN FILE CA (1907 TO DATE)

18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

732 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN

RN 169590-42-5 REGISTRY

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide

CN Celebrex

CN Celecoxib

CN Celocoxib

CN SC 58635

CN YM 177

FS 3D CONCORD

DR 184007-95-2, 194044-54-7

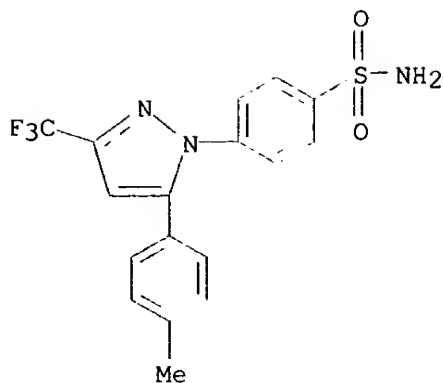
MF C17 H14 F3 N3 O2 S

CI COM

SR US Adopted Names Council

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IPA, MEDLINE, MRCK\*, PHAR, PHARMASEARCH, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

652 REFERENCES IN FILE CA (1907 TO DATE)

17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

663 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil medl; d que 112

FILE 'MEDLINE' ENTERED AT 09:19:42 ON 22 OCT 2003

FILE LAST UPDATED: 21 OCT 2003 (20031021/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4	3187	SEA	FILE=MEDLINE	ABB=ON	CAMPTOTHECIN/CT = Irinotecan	(D) Prevention & control drug therapy
L7	208424	SEA	FILE=MEDLINE	ABB=ON	C4./CT(L) (PC OR DT)/CT = Neoplasms	
L9	2855	SEA	FILE=MEDLINE	ABB=ON	L4(L) (AD OR PD OR PK OR TU)/CT	
L10	317	SEA	FILE=MEDLINE	ABB=ON	L7/MAJ AND L9/MAJ	
L11	967243	SEA	FILE=MEDLINE	ABB=ON	GENERAL REVIEW/DT	
L12	68	SEA	FILE=MEDLINE	ABB=ON	L11 AND L10	

AD = administration & dosage  
PD = pharmacology  
PK = pharmacokinetics  
TU = therapeutic use

=> d iall 112 58-68 ten oldest references

L12 ANSWER 58 OF 68 MEDLINE on STN  
 ACCESSION NUMBER: 1999130870 MEDLINE  
 DOCUMENT NUMBER: 99130870 PubMed ID: 9932078  
 TITLE: [Topoisomerases I: new targets for the treatment of cancer and mechanisms of resistance].  
 Les topo-isomereses I: nouvelles cibles pour le traitement des cancers et mecanismes de resistance.  
 AUTHOR: Pourquier P; Pommier Y  
 CORPORATE SOURCE: Laboratory of Molecular Pharmacology, National Cancer Institute, Bethesda, MD 20892-4255, USA.  
 SOURCE: BULLETIN DU CANCER, (1998 Dec) Spec No 5-10. Ref: 29  
 Journal code: 0072416. ISSN: 0007-4551.  
 PUB. COUNTRY: France  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: French  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199902  
 ENTRY DATE: Entered STN: 19990301  
 Last Updated on STN: 19990301  
 Entered Medline: 19990216

#### ABSTRACT:

DNA topoisomerases I are ubiquitous enzymes that play a crucial role in DNA condensation, replication, transcription, and repair. Eukaryotic enzymes are highly conserved and specifically targeted by natural anticancer agents such as camptothecin and its derivatives. These drugs poison top 1 by inhibiting the enzyme via trapping of top 1 clivage complexes, which ultimately generate cell death. New camptothecin derivatives with better pharmacologic characteristics are under development. Understanding top 1 functions and structure will help to discover more specific and less toxic top 1 inhibitors in order to circumvent drug resistance.

CONTROLLED TERM: Check Tags: Human  
 \*Antineoplastic Agents: PD, pharmacology  
 Antineoplastic Agents: TU, therapeutic use  
 Benzimidazoles: PD, pharmacology  
 Binding Sites: DE, drug effects

Camptothecin: AA, analogs & derivatives  
 \*Camptothecin: PD, pharmacology  
 Camptothecin: TU, therapeutic use  
 DNA Replication: DE, drug effects  
 \*DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
 DNA Topoisomerases, Type I: CH, chemistry  
 DNA Topoisomerases, Type I: PH, physiology  
 DNA, Neoplasm: BI, biosynthesis  
 Drug Design  
 Drug Resistance, Neoplasm  
 Drug Screening Assays, Antitumor  
 English Abstract  
 \*Enzyme Inhibitors: PD, pharmacology  
 Enzyme Inhibitors: TU, therapeutic use  
 Intercalating Agents: PD, pharmacology  
 Macromolecular Systems  
 \*Neoplasm Proteins: AI, antagonists & inhibitors  
 Neoplasm Proteins: PH, physiology  
 \*Neoplasms: DT, drug therapy  
 Neoplasms: EN, enzymology  
 CAS REGISTRY NO.: 7689-03-4 (Camptothecin)  
 CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Benzimidazoles); 0 (DNA, Neoplasm); 0 (Enzyme Inhibitors); 0 (Intercalating Agents); 0 (Macromolecular Systems); 0 (Neoplasm Proteins); EC 5.99.1.2 (DNA Topoisomerases, Type I)

L12 ANSWER 59 OF 68 MEDLINE on STN  
 ACCESSION NUMBER: 1999109498 MEDLINE  
 DOCUMENT NUMBER: 99109498 PubMed ID: 9893620  
 TITLE: Camptothecins: a review of their development and schedules of administration.  
 AUTHOR: O'Leary J; Muggia F M  
 CORPORATE SOURCE: NYU Medical Center, New York, New York 10016, USA.  
 SOURCE: EUROPEAN JOURNAL OF CANCER, (1998 Sep) 34 (10) 1500-8.  
 Ref: 113  
 Journal code: 9005373. ISSN: 0959-8049.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199901  
 ENTRY DATE: Entered STN: 19990209  
 Last Updated on STN: 19990209  
 Entered Medline: 19990125

## ABSTRACT:

Used for centuries in traditional Chinese medicine, camptothecin was rediscovered in the 1950s during a search for compounds that could be used as a source for steroid synthesis. Due to its limited water solubility, a sodium salt was used in the early clinical trials. The severe toxicity and erratic absorption relegated this compound to the research laboratory until the 1980s when the topoisomerase enzyme was identified as the cellular target of camptothecin, the topoisomerase enzyme was found to be overexpressed in cancer cells and a structure-activity relationship was determined for camptothecin. These new developments brought the camptothecins back to the clinical setting for further testing. The various analogues that have been most studied to date include: irinotecan (CPT-11), and its derivative SN-38, topotecan, and 9-aminocamptothecin. Numerous trials have been conducted in an attempt to establish the efficacy in various tumour types, to determine the dose-limiting toxicity and to define the optimal schedule of administration. It seems that large doses of these drugs given on intermittent schedules are not effective. Our hypothesis is that the camptothecins require a prolonged schedule of

administration given continuously at low doses or frequent intermittent dosing schedules to be most effective. With these schedules, normal haematopoietic cells and mucosal progenitor cells with low topoisomerase I levels may be spared, while efficacy is preserved.

CONTROLLED TERM: Check Tags: Human  
\*Antineoplastic Agents, Phytogenic: AD, administration & dosage  
Antineoplastic Agents, Phytogenic: ME, metabolism  
\*Camptothecin: AD, administration & dosage  
Camptothecin: AA, analogs & derivatives  
Camptothecin: ME, metabolism  
DNA Topoisomerases, Type I: ME, metabolism  
Drug Administration Schedule  
\*Neoplasms: DT, drug therapy  
Neoplasms: EN, enzymology  
Topotecan: AD, administration & dosage  
Topotecan: ME, metabolism  
CAS REGISTRY NO.: 100286-90-6 (irinotecan); 123948-87-8 (Topotecan);  
7689-03-4 (Camptothecin)  
CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic); EC 5.99.1.2 (DNA  
Topoisomerases, Type I)

L12 ANSWER 60 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 1998451157 MEDLINE  
DOCUMENT NUMBER: 98451157 PubMed ID: 9779877  
TITLE: The clinical pharmacology of topoisomerase I inhibitors.  
AUTHOR: Abang A M  
CORPORATE SOURCE: University of Oklahoma Health Sciences Center, Oklahoma  
City 73190, USA.  
SOURCE: SEMINARS IN HEMATOLOGY, (1998 Jul) 35 (3 Suppl 4) 13-21.  
Ref: 39  
Journal code: 0404514. ISSN: 0037-1963.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199901  
ENTRY DATE: Entered STN: 19990115  
Last Updated on STN: 19990115  
Entered Medline: 19990104

## ABSTRACT:

The Chinese tree *Camptotheca acuminata*, or Xi Shu, brings us a unique class of chemotherapeutic agents known as the camptothecins. Because the parent compound exhibited excessive toxicity and poor aqueous solubility, synthetic and semisynthetic analogs were developed. These compounds contain a lactone ring that is necessary for activity and is easily hydrolyzed into the less active hydroxy carboxylic acid. Irinotecan, a semisynthetic analog is a prodrug that is cleaved by a carboxylesterase-converting enzyme to form the biologically active metabolite SN-38. The half-lives of irinotecan and SN-38 are relatively long, and both are commonly found in the lactone form. Topotecan differs from irinotecan in that it is found predominately in the inactive carboxylate form at neutral pH, but can be maintained in the lactone form at a lower pH. In phase I clinical trials, the antitumor activity of topotecan has been impressive. In vitro and in vivo studies have shown that combinations between topotecan and 5-fluorouracil or cisplatin have synergistic antitumor effects compared with topotecan alone. Two relatively new agents, 9-aminocamptothecin and GG211, have produced promising results against a variety of tumors.

CONTROLLED TERM: Check Tags: Human  
\*Antineoplastic Agents: PD, pharmacology  
Antineoplastic Agents: TU, therapeutic use

Camptothecin: AA, analogs & derivatives

\*Camptothecin: PD, pharmacology

Camptothecin: TU, therapeutic use

Clinical Trials

\*DNA Topoisomerases, Type I: AI, antagonists & inhibitors

\*Enzyme Inhibitors: PD, pharmacology

Enzyme Inhibitors: TU, therapeutic use

\*Neoplasms: DT, drug therapy

CAS REGISTRY NO.: 7689-03-4 (Camptothecin)

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Enzyme Inhibitors); EC  
5.99.1.2 (DNA Topoisomerases, Type I)

L12 ANSWER 61 OF 68

MEDLINE on STN

ACCESSION NUMBER: 97149817 MEDLINE

DOCUMENT NUMBER: 97149817 PubMed ID: 8996611

TITLE: Design of topoisomerase inhibitors to overcome  
MDR1-mediated drug resistance.

AUTHOR: Chen A Y; Liu L F

CORPORATE SOURCE: Department of Pharmacology, University of Medicine and  
Dentistry of New Jersey, Robert Wood Johnson Medical  
School, Piscataway 08854, USA.

CONTRACT NUMBER: CA39662 (NCI)

SOURCE: ADVANCES IN PHARMACOLOGY, (1994) 29B 245-56. Ref: 30  
Journal code: 9015397. ISSN: 1054-3589.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199704

ENTRY DATE: Entered STN: 19970424

Last Updated on STN: 19970424

Entered Medline: 19970417

#### ABSTRACT:

Human colon tumor xenografts are known to be refractory to most chemotherapeutic anticancer drugs. Recent studies have demonstrated that a class of topoisomerase I inhibitors, camptothecins, exhibits unprecedented antitumor activity against human colon tumor xenografts in nude mice (Giovannella et al., 1989; Potmesil et al., 1991). The ability of camptothecin to overcome MDR1-mediated resistance may be one important contributing factor to camptothecin's impressive activity (Chen et al., 1991). If this interpretation is correct, it will be promising to develop new drugs that can overcome MDR1-mediated resistance for treating certain human solid tumors. Admittedly, MDR1-mediated resistance is only one of the many mechanisms of drug resistance in tumor cells. Designing new drugs for various resistance tumors will require fundamental information on various drug resistance mechanisms. It will eventually be possible to tailor drugs for particular drug-resistant tumors. Using topoisomerase inhibitors, we have begun to understand some of the parameters that may have to be considered for rational drug design.

CONTROLLED TERM: Check Tags: Animal; Comparative Study; Human; Support,  
Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

\*Antineoplastic Agents: TU, therapeutic use

\*Camptothecin: TU, therapeutic use

\*Carcinoma: DT, drug therapy

\*Colonic Neoplasms: DT, drug therapy

\*DNA Topoisomerases, Type I: AI, antagonists & inhibitors

\*DNA Topoisomerases, Type II: AI, antagonists & inhibitors  
Drug Design

Drug Resistance, Neoplasm: GE, genetics

\*Genes, MDR: DE, drug effects

Mice

Mice, Nude

CAS REGISTRY NO.: 7689-03-4 (Camptothecin)  
CHEMICAL NAME: 0 (Antineoplastic Agents); EC 5.99.1.2 (DNA Topoisomerases, Type I); EC 5.99.1.3 (DNA Topoisomerases, Type II)

L12 ANSWER 62 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 97146655 MEDLINE  
DOCUMENT NUMBER: 97146655 PubMed ID: 8993511  
TITLE: Protocols for the treatment of human tumor xenografts with camptothecins.  
AUTHOR: Giovannella B C; Natelson E; Harris N; Vardeman D; Stehlin J S  
CORPORATE SOURCE: Stehlin Foundation for Cancer Research, St. Joseph Hospital, Houston, Texas 77003, USA.  
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1996 Dec 13) 803 181-7. Ref: 15  
Journal code: 7506858. ISSN: 0077-8923.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199701  
ENTRY DATE: Entered STN: 19970219  
Last Updated on STN: 19970219  
Entered Medline: 19970129

## ABSTRACT:

Thirty-five human tumors of various histological types xenografted at various sites into nude mice and rats have been used to assess the anticancer activity of camptothecin and derivatives administered by different routes (subcutaneous, intramuscular, intravenous, intrastomach, and transdermal). Camptothecins are active against human tumors at every site including the brain. So far, the best anticancer/toxicity ratio has been found with 9-nitrocamptothecin (9NC) and 9-aminocamptothecin (9AC) to which 9NC converts in the body of mammals. Comparing the results obtained during clinical trials with the animal ones, it is evident that camptothecins are much less active in humans than in mice against human tumors. This is probably due to the fact that in humans the lactone ring of camptothecins opens much faster than in mice. Measurement of the area under the curve (AUC) in mice and humans under comparable conditions of administration gives values of 3% closed lactone for man versus 55% in mice for 9NC. Clearly this is the crucial problem to overcome in order to improve the efficacy of the camptothecins as anticancer agents.

CONTROLLED TERM: Check Tags: Animal; Human  
Antineoplastic Agents, Phytogenic: PK, pharmacokinetics  
\*Antineoplastic Agents, Phytogenic: TU, therapeutic use  
Camptothecin: AA, analogs & derivatives  
**Camptothecin: PK, pharmacokinetics**  
**\*Camptothecin: TU, therapeutic use**  
Clinical Protocols  
Disease Models, Animal  
Mice  
Mice, Nude  
Neoplasm Transplantation  
**\*Neoplasms, Experimental: DT, drug therapy**  
Rats  
Transplantation, Heterologous  
CAS REGISTRY NO.: 7689-03-4 (Camptothecin)  
CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic)

L12 ANSWER 63 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 97088813 MEDLINE  
DOCUMENT NUMBER: 97088813 PubMed ID: 8934721  
TITLE: The suitability of selected new anticancer agents for

infusional therapy and the effects of others on infusional therapy practices.

AUTHOR: Rowinsky E K

CORPORATE SOURCE: Division of Pharmacology and Experimental Therapeutics, Johns Hopkins Oncology Centre, Baltimore, Maryland 21287-8934, USA.

SOURCE: JOURNAL OF INFUSIONAL CHEMOTHERAPY, (1995 Fall) 5 (4) 173-8. Ref: 60

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19970219  
Last Updated on STN: 19970219  
Entered Medline: 19970122

ABSTRACT:  
The comprehensive development of new antineoplastic agents mandates a thorough evaluation of schedule-dependent cytotoxicity and toxicity. This report focuses on the topoisomerase I inhibitors as an example of a novel class of anticancer agents in exposure duration may be a critical factor in the achievement of an optimal therapeutic index. The mechanistic and pharmacologic determinants and rationale for using protracted exposure schedules in administering several topoisomerase I inhibitors are discussed. The review also discusses dihydropyrimidine dehydrogenase as a pharmacologic target, enabling administration of oral fluoropyrimidines.

CONTROLLED TERM: Check Tags: Comparative Study; Human  
Administration, Oral  
\*Antineoplastic Agents, Phytogenic: AD, administration & dosage  
\*Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use  
\*Camptothecin: AD, administration & dosage  
\*Camptothecin: AA, analogs & derivatives  
\*DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
\*Drug Delivery Systems  
Enzyme Inhibitors: AD, administration & dosage  
Fluorouracil: AD, administration & dosage  
Infusions, Parenteral  
\*Neoplasms: DT, drug therapy  
Oxidoreductases: AI, antagonists & inhibitors  
Uracil: AD, administration & dosage  
Uracil: AA, analogs & derivatives

CAS REGISTRY NO.: 51-21-8 (Fluorouracil); 59989-18-3 (5-ethynyluracil); 66-22-8 (Uracil); 7689-03-4 (Camptothecin)

CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic); 0 (Antineoplastic Combined Chemotherapy Protocols); 0 (Enzyme Inhibitors); EC 1. (Oxidoreductases); EC 1.3.1.2 (dihydrouracil dehydrogenase(NADP)); EC 5.99.1.2 (DNA Topoisomerases, Type I)

L12 ANSWER 64 OF 68 MEDLINE on STN

ACCESSION NUMBER: 96363438 MEDLINE

DOCUMENT NUMBER: 96363438 PubMed ID: 8719971

TITLE: Molecular, cellular, and clinical aspects of the pharmacology of 20(S)camptothecin and its derivatives.

AUTHOR: Rivory L P; Robert J

CORPORATE SOURCE: University of Bordeaux II, Bordeaux, France.

SOURCE: PHARMACOLOGY AND THERAPEUTICS, (1995) 68 (2) 269-96. Ref: 170

JOURNAL code: 7905840. ISSN: 0163-7258.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199609  
ENTRY DATE: Entered STN: 19961008  
Last Updated on STN: 19961008  
Entered Medline: 19960925

## ABSTRACT:

The discovery of the plant alkaloid 20(S)camptothecin (CPT), which displayed potent antitumor activity in preclinical trials, has led to the identification of a novel target of cancer chemotherapy: the nuclear enzyme topoisomerase I. The mechanism by which CPT induces cytotoxicity is the topic of continued research, but appears to be mediated by the stabilisation of transient "cleavable" topoisomerase I-DNA complexes. The pharmacology of CPT and its derivatives is complicated by the apparent requirement of an alpha-hydroxy-delta-lactone ring, which, unfortunately, is hydrolysed reversibly to form inactive carboxylates. Recent research has shown that the extent of hydrolysis in vivo varies between the various derivatives and that this may be an important factor in determining antitumoral activity. In this review, we discuss recent developments in our understanding of the molecular, cellular, and clinical pharmacology of CPT and several of the more promising derivatives.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't  
\*Antineoplastic Agents, Phytogenic: PD, pharmacology  
\*Camptothecin: AA, analogs & derivatives  
\***Camptothecin: PD, pharmacology**  
DNA: ME, metabolism  
\*DNA Topoisomerases, Type I: ME, metabolism  
Drug Resistance, Neoplasm  
\***Neoplasms: DT, drug therapy**  
Neoplasms: ME, metabolism  
CAS REGISTRY NO.: 7689-03-4 (Camptothecin); 9007-49-2 (DNA)  
CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic); EC 5.99.1.2 (DNA Topoisomerases, Type I)

L12 ANSWER 65 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 96316849 MEDLINE  
DOCUMENT NUMBER: 96316849 PubMed ID: 8695345  
TITLE: Current perspectives on camptothecins in cancer treatment.  
AUTHOR: Dancey J; Eisenhauer E A  
SOURCE: BRITISH JOURNAL OF CANCER, (1996 Aug) 74 (3) 327-38. Ref: 146  
Journal code: 0370635. ISSN: 0007-0920.  
PUB. COUNTRY: SCOTLAND: United Kingdom  
DOCUMENT TYPE: Editorial  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199609  
ENTRY DATE: Entered STN: 19960912  
Last Updated on STN: 19980206  
Entered Medline: 19960903

## ABSTRACT:

The camptothecins are a new class of chemotherapeutic agents which have a novel mechanism of action targeting the nuclear enzyme topoisomerase I. Knowledge of the structure-activity relationships of the parent compound camptothecin has led to the development of effective soluble analogues with manageable toxicities. Broad anti-tumour activity shown in preclinical studies has been

confirmed in phase I/II studies for irinotecan and topotecan. Two other derivatives, 9-aminocamptothecin and GI 147211C, are undergoing phase I and early phase II evaluation. Although camptothecin is a plant extract, it and most of its derivatives are not affected by the classic P-gpMDR1 mechanism of resistance which may allow the development of novel combination chemotherapeutic regimens. Important areas of future endeavour will include the development of rational combination regimens and the pursuit of randomised trials. Based on single agent data, colorectal cancer and non-small-cell lung cancer should be the focus for future irinotecan studies. Small-cell lung cancer and ovarian carcinoma are logical tumour types to pursue with topotecan. Both 9-aminocamptothecin and GI 147211C are too early in their clinical evaluation to make recommendations about their future rôles. Finally, the unfolding story of camptothecin analogue development will give important insights into the predictive value of preclinical observations on relative efficacy, schedule dependency, combination strategies and resistance mechanisms which have helped determine the strategies for clinical evaluation of these agents.

CONTROLLED TERM: Check Tags: Human  
\*Antineoplastic Agents, Phytogenic: TU, therapeutic use  
Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use  
Camptothecin: AA, analogs & derivatives  
\*Camptothecin: TU, therapeutic use  
DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
Drug Resistance  
\*Neoplasms: DT, drug therapy  
Topotecan

CAS REGISTRY NO.: 100286-90-6 (irinotecan); 123948-87-8 (Topotecan);  
7689-03-4 (Camptothecin); 86639-63-6 (9-amino-20-camptothecin)

CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic); 0 (Antineoplastic Combined Chemotherapy Protocols); EC 5.99.1.2 (DNA Topoisomerases, Type I)

L12 ANSWER 66 OF 68 MEDLINE on STN

ACCESSION NUMBER: 96135310 MEDLINE

DOCUMENT NUMBER: 96135310 PubMed ID: 8551794

TITLE: The water-insoluble camptothecin analogues: promising drugs for the effective treatment of haematological malignancies.

AUTHOR: Pantazis P

CORPORATE SOURCE: Stehlin Foundation for Cancer Research, St. Joseph Hospital, Houston, Texas, USA.

SOURCE: LEUKEMIA RESEARCH, (1995 Nov) 19 (11) 775-88. Ref: 151  
Journal code: 7706787. ISSN: 0145-2126.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199602

ENTRY DATE: Entered STN: 19960306  
Last Updated on STN: 19970203  
Entered Medline: 19960221

## ABSTRACT:

After failing to exhibit benefits in clinical studies with cancer patients in the early 1970s, camptothecin (CPT) and its water-insoluble analogues are re-emerging as promising drugs with multiple actions in the treatment of human haematological malignancies. CPT analogues interfere with the mechanism of action of the nuclear enzyme topoisomerase I, while the cells progress through the S-phase of the cell cycle and this results in cell death by apoptosis. Modulations of topoisomerase I phosphorylation may indirectly modulate the cytotoxic activity of CPT analogues. In vitro, CPT analogues have exhibited

increased or unaltered killing activity against leukaemia cells resistant to epipodophyllotoxins, anthracyclines, anthracenediones, and Vinca alkaloids, while development of resistance to CPT analogues renders leukaemia and lymphoma cells more sensitive to topoisomerase II-directed drugs, inducers of cell differentiation, and immunotoxins. Oral administration of the CPT analogues has circumvented the inconvenience of solubility of these drugs. Metabolic conversion of the CPT analogue 9-nitro-CPT to equally or more potent 9-amino-CPT practically makes unnecessary treatment of the patient with 9-amino-CPT, which, in addition, is costlier to prepare than 9-nitro-CPT. Considering the therapeutic, economic and handling viewpoints, the overall conclusion is that the water-insoluble CPT analogues are very promising antileukaemia/antilymphoma agents that warrant further preclinical and clinical studies.

CONTROLLED TERM: Check Tags: Animal; Human; Support, Non-U.S. Gov't  
Antineoplastic Agents, Phytogenic: PK, pharmacokinetics  
\*Antineoplastic Agents, Phytogenic: PD, pharmacology  
Antineoplastic Combined Chemotherapy Protocols: PD,  
pharmacology  
Apoptosis: DE, drug effects  
Biotransformation  
\*Camptothecin: AA, analogs & derivatives  
Camptothecin: PK, pharmacokinetics  
\*Camptothecin: PD, pharmacology  
Cell Differentiation: DE, drug effects  
DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
DNA Topoisomerases, Type I: ME, metabolism  
Drug Resistance, Neoplasm  
\*Leukemia: DT, drug therapy  
Leukemia: PA, pathology  
Leukemia, Experimental: PA, pathology  
\*Lymphoma: DT, drug therapy  
Lymphoma: PA, pathology  
Mice  
Phosphorylation  
Solubility  
Tumor Cells, Cultured: DE, drug effects  
Tumor Cells, Cultured: PA, pathology  
CAS REGISTRY NO.: 7689-03-4 (Camptothecin)  
CHEMICAL NAME: 0 (Antineoplastic Agents, Phytogenic); 0 (Antineoplastic  
Combined Chemotherapy Protocols); EC 5.99.1.2 (DNA  
Topoisomerases, Type I)

L12 ANSWER 67 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 96018114 MEDLINE  
DOCUMENT NUMBER: 96018114 PubMed ID: 7551927  
TITLE: Camptothecin analogues in the treatment of non-small cell  
lung cancer.  
AUTHOR: Ardizzoni A  
CORPORATE SOURCE: Department of Medical Oncology I, Istituto Nazionale per la  
Ricerca sul Cancro, Genoa, Italy.  
SOURCE: LUNG CANCER, (1995 Apr) 12 Suppl 1 S177-85. Ref: 19  
Journal code: 8800805. ISSN: 0169-5002.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199510  
ENTRY DATE: Entered STN: 19951227  
Last Updated on STN: 19980206  
Entered Medline: 19951030  
ABSTRACT:

Camptothecin is a natural product derived from the Oriental tree *Camptotheca acuminata* which has shown activity in a number of experimental tumors. Its clinical development was halted in the early-70s owing to its unpredictable and formidable toxicities. Two water-soluble camptothecin analogs have been synthesized recently and are currently in clinical trials: topotecan and CPT-11. Camptothecin and its derivatives are unique in that they represent the only family of topoisomerase I inhibitors. Topoisomerase I is a nuclear enzyme which modulates the topological structure of DNA by making transient single-stranded breaks. Pre-clinical studies have shown that CPT-11 and topotecan possess high and broad antitumor activity against a variety of experimental tumors including both non-small cell lung cancer (NSCLC) and small cell lung cancer. Lack of cross-resistance with most classical anticancer agents has been also demonstrated. Phase I studies have identified neutropenia to be the dose-limiting toxicity for topotecan while, for CPT-11, either neutropenia or diarrhoea were dose-limiting. Maximum Tolerated Doses (MTD) of both agents are greatly dependent upon the schedule used. A Phase II Japanese study of CPT-11 in advanced untreated NSCLC has been recently published. Given at the dose of 100 mg/m<sup>2</sup> as a 90-min infusion, CPT-11 produced a 32% objective response rate out of 72 assessable untreated patients. Similar studies are in progress with topotecan. The same Japanese group has completed Phase I-II studies on the combination of CPT-11 with cisplatin. The optimal dose of CPT-11, which can be safely combined with cisplatin 80 mg/m<sup>2</sup>, was found to be 60 mg/m<sup>2</sup>. (ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Human  
Antineoplastic Agents: CH, chemistry  
\*Antineoplastic Agents: TU, therapeutic use  
\*Camptothecin: AA, analogs & derivatives  
Camptothecin: CH, chemistry  
\*Camptothecin: TU, therapeutic use  
\*Carcinoma, Non-Small-Cell Lung: DT, drug therapy  
Clinical Trials, Phase I  
Drug Evaluation, Preclinical  
\*Lung Neoplasms: DT, drug therapy  
Topotecan  
CAS REGISTRY NO.: 123948-87-8 (Topotecan); 7689-03-4 (Camptothecin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

L12 ANSWER 68 OF 68 MEDLINE on STN  
ACCESSION NUMBER: 93104043 MEDLINE  
DOCUMENT NUMBER: 93104043 PubMed ID: 1361358  
TITLE: New anticancer agents: taxol, camptothecin analogs, and anthracyclines.  
COMMENT: Erratum in: Oncology (Huntingt) 1993 Mar;7(3):105  
AUTHOR: Hawkins M J  
CORPORATE SOURCE: Department of Medicine, Georgetown University Medical Center, Lombardi Cancer Research Center, Washington, DC.  
SOURCE: ONCOLOGY, (1992 Dec) 6 (12) 17-23; discussion 27-30. Ref: 52  
Journal code: 8712059. ISSN: 0890-9091.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199301  
ENTRY DATE: Entered STN: 19930212  
Last Updated on STN: 19950206  
Entered Medline: 19930128

ABSTRACT:  
Taxol, an agent with a unique mechanism of action, has been shown to be highly active in patients with refractory ovarian cancer and may well have significant activity in other malignancies such as breast and lung cancer. The

camptothecin analogs, another unique class of agents, have demonstrated antitumor activity in phase I and II trials. Finally, the anthrapyrazoles are intercalating agents with clinical activity in breast cancer and a toxicity profile that may permit increased dose intensity using colony-stimulating factor support. While this review focuses on these three drug classes, a number of other agents with apparently unique mechanisms of antitumor activity and unusual dose-limiting toxicities are in earlier development. These include antimetabolites; inhibitors of DNA, RNA, or protein synthesis; differentiating agents; agents that inhibit tumor growth by binding to growth factors; and agents whose mechanism of action is best classified as unknown.

CONTROLLED TERM: Check Tags: Female; Human  
 Antibiotics, Anthracycline: AE, adverse effects  
 Antibiotics, Anthracycline: ME, metabolism  
 \*Antibiotics, Anthracycline: PD, pharmacology  
 Antibiotics, Anthracycline: TU, therapeutic use  
 Antibiotics, Antineoplastic: AE, adverse effects  
 Antibiotics, Antineoplastic: ME, metabolism  
 \*Antibiotics, Antineoplastic: PD, pharmacology  
 Antibiotics, Antineoplastic: TU, therapeutic use  
 Breast Neoplasms: DT, drug therapy  
 Camptothecin: AE, adverse effects  
 \*Camptothecin: AA, analogs & derivatives  
 Camptothecin: ME, metabolism  
 Camptothecin: PK, pharmacokinetics  
 \*Camptothecin: PD, pharmacology  
 Clinical Trials, Phase II  
 \*Ovarian Neoplasms: DT, drug therapy  
 Paclitaxel: AE, adverse effects  
 Paclitaxel: ME, metabolism  
 Paclitaxel: PK, pharmacokinetics  
 \*Paclitaxel: PD, pharmacology  
 Paclitaxel: TU, therapeutic use  
 CAS REGISTRY NO.: 33069-62-4 (Paclitaxel); 7689-03-4 (Camptothecin);  
 91440-30-1 (anthrapyrazole)  
 CHEMICAL NAME: 0 (Antibiotics, Anthracycline); 0 (Antibiotics,  
 Antineoplastic)

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L2 1 SEA FILE=REGISTRY ABB=ON GELECOXIB/CN  
 L5 675 SEA FILE=MEDLINE ABB=ON L2  
 L6 8161 SEA FILE=MEDLINE ABB=ON CYCLOOXYGENASE INHIBITORS/CT  
 L7 208424 SEA FILE=MEDLINE ABB=ON C4./CT(L) (PC OR DT)/CT  
 L11 967243 SEA FILE=MEDLINE ABB=ON GENERAL REVIEW/DT  
 L13 5618 SEA FILE=MEDLINE ABB=ON L6(L) (TU OR AD OR PD OR PK)/CT  
 L14 64 SEA FILE=MEDLINE ABB=ON L5 AND L13 AND L7  
 L15 17 SEA FILE=MEDLINE ABB=ON L11 AND L14

=> d iall 115 1-17

L15 ANSWER 1 OF 17 MEDLINE on STN  
 ACCESSION NUMBER: 2003336621 MEDLINE  
 DOCUMENT NUMBER: 22750927 PubMed ID: 12868200  
 TITLE: [Coxibs: highly selective cyclooxygenase-2 inhibitors. Part  
 I. Clinical efficacy].  
 Koksiby--wysoce selektywne inhibitory cyklooksygenazy-2.  
 Czesc I. Aktywnosc kliniczna.  
 AUTHOR: Burdan Franciszek; Korobowicz Agnieszka  
 CORPORATE SOURCE: Pracownia Teratologii Doswiadczalnej, Katedrze i Zakladzie  
 Anatomii Prawidlowej Czlowieka Akademii Medycznej w  
 Lublinie.. fb3@wp.pl  
 SOURCE: POLSKI MERKURIUSZ LEKARSKI, (2003 Apr) 14 (82) 348-51.

Ref: 35  
Journal code: 9705469. ISSN: 1426-9686.  
PUB. COUNTRY: Poland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, ACADEMIC)  
LANGUAGE: Polish  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030719  
Last Updated on STN: 20030925  
Entered Medline: 20030924

## ABSTRACT:

Slow, time-dependent, irreversible, highly selective inhibitors of COX-2 (coxibs) have been used for the treatment of osteoarthritis and rheumatoid arthritis, as well as other disease entities such as acute pain, fever, neoplastic changes, and Alzheimer's disease, the pathomechanism of which is dependent on the coexisting inflammatory process or overexpression of cyclo-oxygenase (COX) genes. The article presents current state of knowledge about the clinical efficacy of coxibs (celecoxib, rofecoxib) compared to non-selective COX inhibitors. The physiology and pathophysiology of both COX isoforms (COX-1, COX-2) are also discussed.

CONTROLLED TERM: Check Tags: Human  
\*Alzheimer Disease: DT, drug therapy  
\***Cyclooxygenase Inhibitors: TU, therapeutic use**  
English Abstract  
\*Fever: DT, drug therapy  
\*Isoenzymes: AI, antagonists & inhibitors  
\***Neoplasms: DT, drug therapy**  
\*Pain: DT, drug therapy  
Prostaglandin-Endoperoxide Synthase  
\*Sulfonamides: PD, pharmacology  
\*Sulfonamides: TU, therapeutic use  
CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 2 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2003272961 MEDLINE  
DOCUMENT NUMBER: 22684337 PubMed ID: 12798395  
TITLE: Carcinogenesis and cyclooxygenase: the potential role of COX-2 inhibition in upper aerodigestive tract cancer.  
AUTHOR: Mohan Sivani; Epstein Joel B  
CORPORATE SOURCE: Department of Oral Medicine, University of Washington, Seattle, WA, USA.  
SOURCE: ORAL ONCOLOGY, (2003 Sep) 39 (6) 537-46. Ref: 131  
Journal code: 9709118. ISSN: 1368-8375.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, ACADEMIC)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030612  
Last Updated on STN: 20030930  
Entered Medline: 20030929

## ABSTRACT:

Cyclooxygenase-2 (COX-2) is upregulated in a number of epithelial cancers, including in upper aerodigestive tract (UADT) premalignant and malignant lesions. The purpose of this review is to provide a comprehensive examination of the potential of COX-2 inhibition in prevention of UADT premalignant and

malignant disease. A Medline and Cancerlit literature search was conducted for the period 1993-2002, and identified literature was reviewed. There is evidence from in vitro studies, as well as animal models, that inhibition of COX-2 may suppress carcinogenesis by affecting a number of pathways of carcinogenesis, promoting apoptosis and inhibiting angiogenesis. Preliminary studies of gastro-intestinal (GI) carcinogenesis suggest that COX-2 inhibitors may represent an approach to the chemoprevention of epithelial cancers. COX-2 inhibitors may have a potential role in chemoprevention of UADT cancer, and clinical trials appear warranted.

CONTROLLED TERM: Check Tags: Animal; Human  
 Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
 Apoptosis  
 \*Carcinoma, Squamous Cell: DT, drug therapy  
 Carcinoma, Squamous Cell: EN, enzymology  
 Carcinoma, Squamous Cell: PA, pathology  
 \*Cyclooxygenase Inhibitors: TU, therapeutic use  
 Enzyme Induction  
 Epithelial Cells: EN, enzymology  
 \*Head and Neck Neoplasms: DT, drug therapy  
 Head and Neck Neoplasms: EN, enzymology  
 Head and Neck Neoplasms: PA, pathology  
 Isoenzymes: ME, metabolism  
 Models, Animal  
 Mouth Neoplasms: DT, drug therapy  
 Mouth Neoplasms: EN, enzymology  
 Mouth Neoplasms: PA, pathology  
 Neovascularization, Pathologic: PC, prevention & control  
 \*Precancerous Conditions: DT, drug therapy  
 Precancerous Conditions: EN, enzymology  
 Precancerous Conditions: PA, pathology  
 Prostaglandin-Endoperoxide Synthase: ME, metabolism  
 Randomized Controlled Trials  
 Sulfonamides: TU, therapeutic use  
 Tumor Markers, Biological: ME, metabolism

CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
 CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Sulfonamides); 0 (Tumor Markers, Biological); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 3 OF 17 MEDLINE on STN  
 ACCESSION NUMBER: 2003208867 MEDLINE  
 DOCUMENT NUMBER: 22615443 PubMed ID: 12730704  
 TITLE: Selective COX-2 inhibitors as chemopreventive and therapeutic agents.  
 AUTHOR: Grossman H Barton  
 CORPORATE SOURCE: Department of Urology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, USA..  
 hbgrossman@mdanderson.org  
 SOURCE: Drugs Today (Barc), (2003 Mar) 39 (3) 203-12. Ref: 74  
 Journal code: 101160518. ISSN: 0025-7656.  
 PUB. COUNTRY: Spain  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200309  
 ENTRY DATE: Entered STN: 20030506  
 Last Updated on STN: 20030905  
 Entered Medline: 20030904

## ABSTRACT:

Selective cyclooxygenase-2 (COX-2) inhibitors have received increasing attention for their role in the prevention and treatment of cancer. Considerable preclinical data support this use. Furthermore, clinical studies have shown that this enzyme is upregulated in a variety of premalignant and malignant states and that its inhibition can decrease colon polyp formation in patients with familial adenomatous polyposis. A number of studies are now investigating the use of COX-2 inhibitors to prevent or treat a number of different cancers. These ongoing trials will determine whether these agents are useful in the treatment of cancer.

CONTROLLED TERM: Check Tags: Animal; Human  
Clinical Trials

**\*Cyclooxygenase Inhibitors: TU, therapeutic use**

**\*Isoenzymes**

Isoenzymes: AI, antagonists & inhibitors

Isoenzymes: ME, metabolism

Isoenzymes: PH, physiology

**\*Neoplasms**

Neoplasms: EN, enzymology

**Neoplasms: PC, prevention & control**

**\*Prostaglandin-Endoperoxide Synthase**

Prostaglandin-Endoperoxide Synthase: ME, metabolism

Prostaglandin-Endoperoxide Synthase: PH, physiology

Sulfonamides: TU, therapeutic use

CAS REGISTRY NO.: **169590-42-5 (celecoxib)**

CHEMICAL NAME: 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 4 OF 17

MEDLINE on STN

ACCESSION NUMBER: 2003059682 MEDLINE

DOCUMENT NUMBER: 22457447 PubMed ID: 12570027

TITLE: Do selective cyclo-oxygenase inhibitors eliminate the adverse events associated with nonsteroidal anti-inflammatory drug therapy?.

AUTHOR: Deviere Jacques

CORPORATE SOURCE: Department of Gastroenterology, University Hospital Erasme, Route de Lennik 808, Brussels 1070, Belgium..  
jdeviere@ulb.ac.be

SOURCE: EUROPEAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (2002 Sep) 14 Suppl 1 S29-33. Ref: 41  
Journal code: 9000874. ISSN: 0954-691X.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

**General Review; (REVIEW)**

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 20030207

Last Updated on STN: 20030306

Entered Medline: 20030305

## ABSTRACT:

Among the most widely prescribed drugs worldwide, non-steroidal anti-inflammatory drugs (NSAIDs) are effective for relieving pain, but they are also associated with a high incidence of gastrointestinal (GI) adverse events. Both the beneficial and harmful effects of NSAIDs result from inhibition of the cyclo-oxygenase (COX) enzyme. Recognition of the two distinct COX isoforms prompted development of drugs that selectively block the activity of COX-2, thus providing pain relief and reducing inflammation while sparing COX-1, the enzyme apparently responsible for most protective prostaglandin synthesis in the mucosa of the stomach and duodenum. The results of preclinical and clinical studies indicate that COX-2 inhibitors exhibit high selectivity in

inhibiting COX-2, provide excellent pain relief, and cause significantly less GI toxicity than do conventional nonselective NSAIDs. Although they represent a significant advance over nonselective NSAIDs, selective COX-2 inhibitors are not without limitations. They do not completely eliminate GI toxicity or the renal side effects associated with use of conventional NSAIDs. Moreover, in cases of inflammation or ulceration in the GI tract, COX-2 inhibition may delay ulcer healing. Finally, case reports and the results of animal experiments suggest that COX-2 inhibitors may adversely affect ovulation and cause a tendency towards prothrombotic events.

CONTROLLED TERM: Check Tags: Human  
 Alzheimer Disease: DT, drug therapy  
 \*Anti-Inflammatory Agents, Non-Steroidal: AE, adverse effects  
 \*Cyclooxygenase Inhibitors: TU, therapeutic use  
 Lactones: TU, therapeutic use  
 Neoplasms: DT, drug therapy  
 Sulfonamides: TU, therapeutic use  
 Thiazines: TU, therapeutic use  
 Thiazoles: TU, therapeutic use

CAS REGISTRY NO.: 169590-42-5 (celecoxib); 51803-78-2 (nimesulide); 71125-38-7 (meloxicam)

CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Cyclooxygenase Inhibitors); 0 (Lactones); 0 (Sulfonamides); 0 (Thiazines); 0 (Thiazoles); 0 (rofecoxib)

L15 ANSWER 5 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2002396091 MEDLINE

DOCUMENT NUMBER: 22140024 PubMed ID: 12145422

TITLE: Chemoprevention in colorectal neoplasias: what is practical and feasible?.

AUTHOR: Ricciardiello Luigi; Roda Enrico; Bazzoli Franco

CORPORATE SOURCE: Dipartimento di Medicina Interna e Gastroenterologia, Universita di Bologna, Italy.

SOURCE: DIGESTIVE DISEASES, (2002) 20 (1) 70-2. Ref: 20  
 Journal code: 8701186. ISSN: 0257-2753.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020730  
 Last Updated on STN: 20021003  
 Entered Medline: 20021002

# ABSTRACT:

Chemoprevention strategies for colorectal cancer have gained increasing attention. Despite contradictory data regarding the use of micronutrients and antioxidant vitamins as chemopreventive tools, the identification of cyclooxygenase 2 (COX-2) upregulation in colorectal adenomas has led to the development of new drugs, named COX-2 inhibitors, that directly target the molecular mechanism of carcinogenesis. Celecoxib, one of the two COX-2 inhibitors available on the market, has been approved for chemoprevention of familial adenomatous polyposis. In the future, we might expect these drugs to be used in the prevention of colon cancer in patients at increased risk, such as those with a positive family history.

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CONTROLLED TERM: Check Tags: Human  
 Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
 Chemoprevention  
 \*Colorectal Neoplasms: PC, prevention & control  
 \*Cyclooxygenase Inhibitors: TU, therapeutic use

Sulfonamides: TU, therapeutic use  
CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Cyclooxygenase Inhibitors); 0 (Sulfonamides)

L15 ANSWER 6 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002331182 MEDLINE  
DOCUMENT NUMBER: 22068842 PubMed ID: 12074318  
TITLE: Reducing the risk of colorectal cancer by intervening in  
the process of carcinogenesis: a status report.  
AUTHOR: Alberts David S  
CORPORATE SOURCE: Cancer Prevention and Control, Arizona Cancer Center,  
University of Arizona, Tucson 85724, USA.  
SOURCE: CANCER JOURNAL, (2002 May-Jun) 8 (3) 208-21. Ref: 128  
Journal code: 100931981, ISSN: 1528-9117.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, ACADEMIC)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200302  
ENTRY DATE: Entered STN: 20020621  
Last Updated on STN: 20030211  
Entered Medline: 20030210

ABSTRACT:  
Risk factors for colorectal cancer have been identified, and significant advances have been made in understanding the process of colorectal carcinogenesis. The transition from normal colonic mucosa to adenomatous polyp to adenocarcinoma is a gradual process involving genetic and epigenetic instability that can take decades, offering numerous opportunities for early detection (e.g., colonoscopy screenings), lifestyle changes (e.g., reduced red meat intake, increased physical activity, and reduced alcohol/ tobacco exposure), and chemopreventive interventions. Aspirin and various other nonsteroidal anti-inflammatory drugs may have chemopreventive benefits for colorectal cancer and other human epithelial carcinomas, but the long-term use of nonsteroidal anti-inflammatory drugs is associated with serious gastrointestinal side effects. Recently, overexpression of cyclooxygenase-2 has been documented in colorectal tumors and numerous other pre-cancers and cancers. The development of selective cyclooxygenase-2 inhibitors, such as celecoxib, provides an opportunity for preventive intervention in the carcinogenic process. Celecoxib has been approved for the management of familial adenomatous polyposis and is under investigation for the management of sporadic colorectal polyps and for its potential as a chemopreventive agent for other cancers.

CONTROLLED TERM: Check Tags: Human  
Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
Clinical Trials, Phase III  
\*Colorectal Neoplasms: PC, prevention & control  
Cyclooxygenase Inhibitors: TU, therapeutic use  
Prognosis  
Risk Factors  
Sulfonamides: TU, therapeutic use  
CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Cyclooxygenase Inhibitors); 0 (Sulfonamides)

L15 ANSWER 7 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002274257 MEDLINE  
DOCUMENT NUMBER: 22009022 PubMed ID: 12014863  
TITLE: Celecoxib with chemotherapy in colorectal cancer.  
AUTHOR: Blanke Charles D

CORPORATE SOURCE: Oregon Health Sciences University, Portland 97201, USA.  
SOURCE: ONCOLOGY, (2002 Apr) 16 (4 Suppl 3) 17-21. Ref: 32  
Journal code: 8712059. ISSN: 0890-9091.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200211  
ENTRY DATE: Entered STN: 20020517  
Last Updated on STN: 20021211  
Entered Medline: 20021107

## ABSTRACT:

Cyclooxygenase-2 (COX-2) is the enzyme that normally synthesizes prostaglandins during an inflammatory response. Many primary and metastatic cancers express COX-2, and its presence is correlated with tumor angiogenesis, more invasive tumor phenotype, resistance to apoptosis, and systemic immunosuppression. The expression of COX-2 is associated with a worse prognosis. Inhibition of prostaglandin synthesis may be beneficial in human malignancy. Regular consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) decreases the incidence of, and mortality rate resulting from, a number of types of gastrointestinal cancers. Premalignant colonic lesions regress following the administration of nonspecific COX inhibitors, such as sulindac (Clinoril). Advanced solid tumor patients treated with indomethacin (Indocin) survive twice as long as do such patients who receive supportive care alone. The U.S. Food and Drug Administration has approved specific COX-2 inhibitors for the treatment of arthritis, pain, and familial adenomatous polyposis. Preclinical studies show that these drugs block angiogenesis, suppress solid tumor metastases, and slow the growth of implanted gastrointestinal cancer cell lines. The COX-2 inhibitors have safely and effectively been combined with chemotherapeutic agents in experimental studies. Ongoing clinical trials are currently assessing the potential therapeutic role of COX-2 inhibitors in both prevention and treatment of a diverse range of human cancers.

CONTROLLED TERM: Check Tags: Human  
\*Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
\*Antineoplastic Agents: TU, therapeutic use  
Clinical Trials  
\*Colorectal Neoplasms: DT, drug therapy  
Colorectal Neoplasms: EN, enzymology  
\*Cyclooxygenase Inhibitors: TU, therapeutic use  
Gene Expression Regulation, Enzymologic  
Gene Expression Regulation, Neoplastic  
\*Isoenzymes: AI, antagonists & inhibitors  
Isoenzymes: ME, metabolism  
Prostaglandin-Endoperoxide Synthase: ME, metabolism  
\*Sulfonamides: TU, therapeutic use  
CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Antineoplastic Agents); 0 (Cyclooxygenase Inhibitors); 0  
(Isoenzymes); 0 (Sulfonamides); EC 1.14.99.-  
(cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-  
Endoperoxide Synthase)

L15 ANSWER 8 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002241414 MEDLINE  
DOCUMENT NUMBER: 21975751 PubMed ID: 11978897  
TITLE: Translational medicine: targetting cyclo-oxygenase isozymes  
to prevent cancer.  
AUTHOR: Sharma R A  
CORPORATE SOURCE: Oncology Department, University of Leicester, Leicester  
Royal Infirmary, UK.. ras20@le.ac.uk

SOURCE: QJM, (2002 May) 95 (5) 267-73. Ref: 43  
Journal code: 9438285. ISSN: 1460-2725.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200206

ENTRY DATE: Entered STN: 20020430  
Last Updated on STN: 20030318  
Entered Medline: 20020625

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't  
Arachidonic Acid: ME, metabolism  
Aspirin: PD, pharmacology  
Aspirin: TU, therapeutic use  
Cardiovascular Diseases: PC, prevention & control  
**Cyclooxygenase Inhibitors: PD, pharmacology**  
**\*Cyclooxygenase Inhibitors: TU, therapeutic use**  
Drug Design  
Isoenzymes: AI, antagonists & inhibitors  
Isoenzymes: ME, metabolism  
Lactones: TU, therapeutic use  
**\*Neoplasms: PC, prevention & control**  
Prostaglandin-Endoperoxide Synthase: ME, metabolism  
Prostaglandins: BI, biosynthesis  
Randomized Controlled Trials  
Sulfonamides: TU, therapeutic use

CAS REGISTRY NO.: **169590-42-5 (celecoxib);** 50-78-2 (Aspirin);  
506-32-1 (Arachidonic Acid)

CHEMICAL NAME: 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0  
(Lactones); 0 (Prostaglandins); 0 (Sulfonamides); 0  
(rofecoxib); EC 1.14.99.- (cyclooxygenase 1); EC 1.14.99.-  
(cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-  
Endoperoxide Synthase)

L15 ANSWER 9 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2002237715 MEDLINE

DOCUMENT NUMBER: 21970483 PubMed ID: 11973925

TITLE: [New anti-inflammatory analgetics--are they needed?].  
Uudet tulehduskipulaakkeet--tarvitaanko niita?.

AUTHOR: Paakkari I

CORPORATE SOURCE: Helsingin yliopiston biolaaketieteen laitos, farmakologian  
ja toksikologian osasto PL 8, 00014 Helsingin yliopisto..  
ilari.paakkari@helsinki.fi

SOURCE: DUODECIM, (1999) 115 (20) 2217-24. Ref: 43  
Journal code: 0373207. ISSN: 0012-7183.

PUB. COUNTRY: Finland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)

LANGUAGE: Finnish

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 20020429  
Last Updated on STN: 20020511  
Entered Medline: 20020510

CONTROLLED TERM: Check Tags: Human  
Anti-Inflammatory Agents, Non-Steroidal: AE, adverse  
effects  
Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology  
**\*Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic  
use**

Colorectal Neoplasms: PC, prevention & control  
Cyclooxygenase Inhibitors: AE, adverse effects  
Cyclooxygenase Inhibitors: PD, pharmacology  
\*Cyclooxygenase Inhibitors: TU, therapeutic use  
Intestinal Mucosa: DE, drug effects  
Isoenzymes: ME, metabolism  
Kidney: DE, drug effects  
Lactones: AE, adverse effects  
Lactones: PD, pharmacology  
Lactones: TU, therapeutic use  
Prostaglandin-Endoperoxide Synthase: ME, metabolism  
Sulfonamides: AE, adverse effects  
Sulfonamides: PD, pharmacology  
Sulfonamides: TU, therapeutic use

CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Lactones);  
0 (Sulfonamides); 0 (rofecoxib); EC 1.14.99.-  
(cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-  
Endoperoxide Synthase)

L15 ANSWER 10 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002227712 MEDLINE  
DOCUMENT NUMBER: 21961581 PubMed ID: 11965228  
TITLE: Celecoxib: a specific COX-2 inhibitor with anticancer  
properties.  
AUTHOR: Koki Alane T; Masferrer Jaime L  
CORPORATE SOURCE: Pharmacia Corporation, Chesterfield, MO 63017, USA..  
alane.t.koki@pharmacia.com  
SOURCE: CANCER CONTROL, (2002 Mar-Apr) 9 (2 Suppl) 28-35. Ref: 106  
Journal code: 9438457. ISSN: 1073-2748.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 20020420  
Last Updated on STN: 20020614  
Entered Medline: 20020613

ABSTRACT:  
In addition to the well-established pathophysiological role that COX-2 plays in inflammation, recent evidence implies that this isoform may also be involved in multiple biologic events throughout the tumorigenic process. Many epidemiological studies demonstrate that nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk of a wide range of tumors. Further, COX-2 is chronically overexpressed in many premalignant, malignant, and metastatic human cancers, and levels of overexpression have been shown to significantly correlate to invasiveness, prognosis, and survival in some cancers. Pharmacological studies consistently demonstrate that COX-2 inhibitors dose-dependently inhibit tumor growth and metastasis in various relevant animal models of cancer. Importantly, several investigators have also shown COX-2 inhibitors may act additively or synergistically with currently used cytotoxics and molecularly targeted agents. Here we present a broad overview of the growing evidence that COX-2 plays a pivotal role throughout oncogenesis and summarize the rationale to explore the use of COX-2 inhibitors for the prevention and/or treatment of cancer as a single agent or in combination with current anticancer modalities.

CONTROLLED TERM: Check Tags: Animal; Human  
\*Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology  
Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic  
use

\*Anticarcinogenic Agents: PD, pharmacology  
\*Antineoplastic Agents: PD, pharmacology  
\*Cyclooxygenase Inhibitors: PD, pharmacology  
Disease Models, Animal  
Gene Expression Regulation, Enzymologic  
Gene Expression Regulation, Neoplastic  
\*Isoenzymes: AI, antagonists & inhibitors  
\*Neoplasms: DT, drug therapy  
Neoplasms: PC, prevention & control  
Prognosis  
Prostaglandin-Endoperoxide Synthase  
Receptor, erbB-2: DE, drug effects  
\*Sulfonamides: PD, pharmacology

CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Anticarcinogenic Agents); 0 (Antineoplastic Agents); 0  
(Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0  
(Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC  
1.14.99.1 (Prostaglandin-Endoperoxide Synthase); EC  
2.7.1.112 (Receptor, erbB-2)

L15 ANSWER 11 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002066421 MEDLINE  
DOCUMENT NUMBER: 21651722 PubMed ID: 11793634  
TITLE: Celecoxib as adjunctive therapy for treatment of colorectal  
cancer.  
AUTHOR: North G L  
CORPORATE SOURCE: School of Pharmacy, University of Montana, Missoula, MT,  
USA.. gnorth@northbay.org  
SOURCE: ANNALS OF PHARMACOTHERAPY, (2001 Dec) 35 (12) 1638-43.  
Ref: 17  
Journal code: 9203131. ISSN: 1060-0280.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW LITERATURE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 20020125  
Last Updated on STN: 20020612  
Entered Medline: 20020611

## ABSTRACT:

OBJECTIVE: To describe the role of celecoxib as adjunctive therapy in the treatment of familial adenomatous polyposis (FAP), an inherited autosomal dominant predisposition syndrome for colorectal cancer. DATA SOURCES: Literature was evaluated through MEDLINE search (1995-March 2000) and through secondary sources, using the search terms celecoxib, cyclooxygenase-2 inhibitors, and familial adenomatous polyps. DATA SYNTHESIS: Observational studies have found a decreased rate of colorectal cancer in people who regularly took aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs). The Food and Drug Administration granted accelerated approval in December 1999 for the NSAID celecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, for adjunctive therapy in patients with FAP, based on a six-month, randomized, controlled clinical trial. CONCLUSIONS: Aspirin and other NSAIDs reduce the incidence of colorectal cancer in the general population. Limited clinical studies in patients with FAP using nonaspirin NSAIDs have shown a reduction in polyp burden. A current clinical trial using celecoxib has also shown a reduction in polyp burden in patients with FAP. The long-term clinical impact of using a selective COX-2 inhibitor is not known, since celecoxib has not been studied beyond six months in patients with FAP. By reducing the polyp burden in FAP patients, celecoxib may be useful as adjunctive chemotherapy, in addition to routine endoscopic surveillance and surgery.

CONTROLLED TERM: Check Tags: Female; Human; Male  
\*Adenomatous Polyposis Coli  
Adenomatous Polyposis Coli: CO, complications  
**Adenomatous Polyposis Coli: DT, drug therapy**  
\*Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
\*Aspirin: TU, therapeutic use  
Chemotherapy, Adjuvant  
\*Colorectal Neoplasms  
**Colorectal Neoplasms: DT, drug therapy**  
Colorectal Neoplasms: ET, etiology  
**Colorectal Neoplasms: PC, prevention & control**  
Cyclooxygenase Inhibitors: AE, adverse effects  
**\*Cyclooxygenase Inhibitors: TU, therapeutic use**  
Randomized Controlled Trials  
Sulfonamides: AE, adverse effects  
\*Sulfonamides: TU, therapeutic use  
CAS REGISTRY NO.: 169590-42-5 (celecoxib); 50-78-2 (Aspirin)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Cyclooxygenase Inhibitors); 0 (Sulfonamides)

L15 ANSWER 12 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002053265 MEDLINE  
DOCUMENT NUMBER: 21637359 PubMed ID: 11779086  
TITLE: Approach to angiogenesis inhibition based on cyclooxygenase-2.  
AUTHOR: Masferrer J  
CORPORATE SOURCE: Pharmacia Corporation, St. Louis, Missouri 63167, USA.  
SOURCE: CANCER JOURNAL, (2001 Nov-Dec) 7 Suppl 3 S144-50. Ref: 38  
Journal code: 100931981. ISSN: 1528-9117.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
**General Review; (REVIEW)**  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200203  
ENTRY DATE: Entered STN: 20020125  
Last Updated on STN: 20020321  
Entered Medline: 20020320

## ABSTRACT:

Two cyclooxygenase (COX) isoforms have been identified: COX-1 and COX-2. COX-1 is the constitutively expressed form of the enzyme and is ubiquitous in its distribution. COX-2 is inducible and is present in inflammatory foci, tumors, and neovasculature. Expression of COX-2 appears to be important in tumor promotion, growth, and metastasis. It is up-regulated in a variety of premalignant disorders and malignancies. COX inhibitors have a major role in the treatment of inflammation and pain. Epidemiologic evidence in patients who take nonsteroidal anti-inflammatory drugs links COX inhibition with decreases in malignant esophageal, stomach, colon, lung, and breast tumors. Nonselective COX inhibitors have demonstrated efficacy in control of familial adenomatous polyposis, a disorder associated with the development of thousands of benign intestinal polyps. The selective COX-2 inhibitor celecoxib (Celebrex, Pharmacia) has been shown to reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis as an adjunct to usual care. Celecoxib has recently been approved for this indication and offers the potential for equivalent or greater efficacy than that seen with nonselective COX inhibitors but without the gastrointestinal mucosal toxicity and the inhibition of platelet function associated with those agents. Angiogenesis is a feature of both benign and malignant disease. Because COX-2 is up-regulated in the neovasculature of the rheumatoid pannus and in malignant tumors and their surrounding stroma, selective COX-2 inhibitors may be able to modify the progression of these disorders through the control of angiogenesis.

CONTROLLED TERM: Check Tags: Animal; Human  
\*Angiogenesis Inhibitors: TU, therapeutic use  
\*Antineoplastic Agents: TU, therapeutic use  
Colonic Neoplasms: DT, drug therapy  
Colonic Neoplasms: EN, enzymology  
\*Cyclooxygenase Inhibitors: TU, therapeutic use  
Isoenzymes: BI, biosynthesis  
Isoenzymes: DE, drug effects  
Neovascularization, Pathologic: PC, prevention & control  
Prostaglandin-Endoperoxide Synthase: BI, biosynthesis  
Prostaglandin-Endoperoxide Synthase: DE, drug effects  
Prostaglandins: ME, metabolism  
\*Sulfonamides: TU, therapeutic use

CAS REGISTRY NO.: 169590-42-5 (celecoxib)  
CHEMICAL NAME: 0 (Angiogenesis Inhibitors); 0 (Antineoplastic Agents); 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Prostaglandins); 0 (Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 13 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002009468 MEDLINE  
DOCUMENT NUMBER: 21235110 PubMed ID: 11336575  
TITLE: Celecoxib: a new option in the treatment of arthropathies and familial adenomatous polyposis.  
AUTHOR: Davies N M; Gudde T W; de Leeuw M A  
CORPORATE SOURCE: Faculty of Pharmacy, University of Sydney, Sydney, New South Wales 2006, Australia.. ndavies@pharm.usyd.edu.au  
SOURCE: Expert Opin Pharmacother, (2001 Jan) 2 (1) 139-52. Ref: 87  
Journal code: 100897346. ISSN: 1465-6566.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200210  
ENTRY DATE: Entered STN: 20020121  
Last Updated on STN: 20021004  
Entered Medline: 20021003

## ABSTRACT:

The discovery of the two isoenzymes of cyclooxygenase (COX) has recently lead to the development and clinical introduction of specific inhibitors of cyclooxygenase-2 (COX-2), such as celecoxib, onto the market. Celecoxib is an effective anti-inflammatory, analgesic and antipyretic agent therapeutically utilised in the management of osteoarthritis and rheumatoid arthritis. In addition, celecoxib has some novel therapeutic and pharmacological activities. Celecoxib inhibits anti-apoptotic kinase activation and is the first specific COX-2 inhibitor to be marketed for familial adenomatous polyposis, an inheritable predisposition for colorectal cancer. Celecoxib is not without gastrointestinal (GI) side effects but demonstrates markedly reduced GI ulceration in clinical trials when compared to traditional non-specific non-steroidal anti-inflammatory drugs (NSAIDs). The specific COX-2 inhibitors each have distinctive pharmacokinetic properties. Celecoxib can be given either once or twice daily. Racial differences in drug disposition, and pharmacokinetic changes in elderly patients, patients with chronic renal insufficiency and patients with mild to moderate hepatic impairment, are evident with celecoxib. Despite the specific action of these drugs, there remains the potential for significant drug interactions. Celecoxib has demonstrated interactions with fluconazole, lithium and warfarin. Increased clinical vigilance should be maintained when co-prescribing medications with celecoxib until further clinical experience is gained. Celecoxib represents a major therapeutic advance in terms of GI safety. However, long-term safety in

other organ systems, safety with concomitant drug administration, and pharmacoeconomic benefits still remain to be proven.

CONTROLLED TERM: Check Tags: Animal; Human

Absorption

**\*Adenomatous Polyposis Coli: DT, drug therapy**

Adenomatous Polyposis Coli: EN, enzymology

**\*Arthritis: DT, drug therapy**

Arthritis: EN, enzymology

Costs and Cost Analysis

Cyclooxygenase Inhibitors: AE, adverse effects

Cyclooxygenase Inhibitors: EC, economics

**Cyclooxygenase Inhibitors: PK, pharmacokinetics**

**\*Cyclooxygenase Inhibitors: TU, therapeutic use**

**\*Isoenzymes: AI, antagonists & inhibitors**

Prostaglandin-Endoperoxide Synthase

Sulfonamides: AE, adverse effects

Sulfonamides: EC, economics

Sulfonamides: PK, pharmacokinetics

**\*Sulfonamides: TU, therapeutic use**

CAS REGISTRY NO.: 169590-42-5 (celecoxib)

CHEMICAL NAME: 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 14 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2001421560 MEDLINE

DOCUMENT NUMBER: 21364013 PubMed ID: 11470927

TITLE: Familiar drugs may prevent cancer.

AUTHOR: Sharma R A; Gescher A J; O'Byrne K J; Steward W P

CORPORATE SOURCE: Oncology Department, University of Leicester, Leicester Royal Infirmary, Leicester LE1 5WW, UK.. ras20@le.ac.uk  
SOURCE: POSTGRADUATE MEDICAL JOURNAL, (2001 Aug) 77 (910) 492-7.  
Ref: 60

Journal code: 0234135. ISSN: 0032-5473.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

**General Review; (REVIEW)**

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 20010917

Last Updated on STN: 20010917

Entered Medline: 20010913

**ABSTRACT:**

Despite positive results in large scale chemoprevention trials, many physicians are unaware of the potential cancer preventive properties of drugs in common usage. The antioestrogen tamoxifen and the selective cyclo-oxygenase-2 inhibitor celecoxib have been licensed in the USA for the chemoprevention of breast and colorectal cancers respectively in selected high risk individuals. Similarly, folate and retinol have been shown to decrease the incidence of colorectal cancer and squamous cell carcinoma of the skin respectively in large scale intervention trials. Other retinoids have proved efficacious in the tertiary chemoprevention of cancers of the breast and head/neck. Epidemiological evidence also exists in favour of aspirin, non-steroidal anti-inflammatory drugs, and angiotensin converting enzyme inhibitors preventing certain cancers. Phytochemicals may represent less toxic alternatives to these agents. Although some of these drugs are available without prescription and most are not yet licensed for use in cancer chemoprevention, physicians and students of medicine should be aware of this accumulating evidence base. Practitioners should be amenable to patient referral to discuss complex issues such as risk estimation or potential benefit from intervention.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use  
\*Anticarcinogenic Agents: TU, therapeutic use  
Aspirin: TU, therapeutic use  
Cyclooxygenase Inhibitors: TU, therapeutic use  
Folic Acid: TU, therapeutic use  
\*Neoplasms: PC, prevention & control  
Raloxifene: TU, therapeutic use  
Sulfonamides: TU, therapeutic use  
Tamoxifen: TU, therapeutic use  
Vitamin A: TU, therapeutic use

CAS REGISTRY NO.: 10540-29-1 (Tamoxifen); 11103-57-4 (Vitamin A);  
169590-42-5 (celecoxib); 50-78-2 (Aspirin); 59-30-3  
(Folic Acid); 84449-90-1 (Raloxifene)

CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0  
(Anticarcinogenic Agents); 0 (Cyclooxygenase Inhibitors); 0  
(Sulfonamides)

L15 ANSWER 15 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2001379145 MEDLINE

DOCUMENT NUMBER: 21329125 PubMed ID: 11435450

TITLE: Cyclooxygenase-selective inhibition of prostanoid  
formation: transducing biochemical selectivity into  
clinical read-outs.

AUTHOR: Patrono C; Patrignani P; Garcia Rodriguez L A

CORPORATE SOURCE: Department of Medicine and Aging, University of Chieti G.  
D'Annunzio School of Medicine, Chieti, Italy..  
cpatrono@unich.it

SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2001 Jul) 108 (1) 7-13.  
Ref: 31  
Journal code: 7802877. ISSN: 0021-9738.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200108

ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

CONTROLLED TERM: Check Tags: Comparative Study; Human; Support, Non-U.S.  
Gov't  
Anti-Inflammatory Agents, Non-Steroidal: AE, adverse effects  
\*Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology  
Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
Anticarcinogenic Agents: PD, pharmacology  
Anticarcinogenic Agents: TU, therapeutic use  
Aspirin: AE, adverse effects  
Aspirin: PD, pharmacology  
Aspirin: TU, therapeutic use  
Blood Platelets: DE, drug effects  
Blood Platelets: EN, enzymology  
Cardiovascular Diseases: EP, epidemiology  
Colorectal Neoplasms: PC, prevention & control  
Cyclooxygenase Inhibitors: AE, adverse effects  
\*Cyclooxygenase Inhibitors: PD, pharmacology  
Cyclooxygenase Inhibitors: TU, therapeutic use  
Depression, Chemical  
Dinoprostone: BI, biosynthesis

Epoprostenol: BI, biosynthesis  
Gastric Mucosa: DE, drug effects  
Gastrointestinal Hemorrhage: CI, chemically induced  
Gastrointestinal Hemorrhage: EP, epidemiology  
Gastrointestinal Hemorrhage: PC, prevention & control  
Incidence  
Intestinal Mucosa: DE, drug effects  
\*Isoenzymes: AI, antagonists & inhibitors  
Isoenzymes: PH, physiology  
Lactones: AE, adverse effects  
Lactones: PD, pharmacology  
Lactones: TU, therapeutic use  
Peptic Ulcer: CI, chemically induced  
Peptic Ulcer: EP, epidemiology  
Peptic Ulcer: PC, prevention & control  
Prostaglandin-Endoperoxide Synthase: PH, physiology  
\*Prostaglandins: BI, biosynthesis  
Randomized Controlled Trials  
Substrate Specificity  
Sulfonamides: AE, adverse effects  
Sulfonamides: PD, pharmacology  
Sulfonamides: TU, therapeutic use  
Thromboembolism: EP, epidemiology  
Thromboembolism: PC, prevention & control  
Thromboxane A2: BI, biosynthesis  
Treatment Outcome

CAS REGISTRY NO.: 169590-42-5 (celecoxib); 35121-78-9  
(Epoprostenol); 363-24-6 (Dinoprostone); 50-78-2 (Aspirin);  
57576-52-0 (Thromboxane A2)  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0  
(Anticarcinogenic Agents); 0 (Cyclooxygenase Inhibitors); 0  
(Isoenzymes); 0 (Lactones); 0 (Prostaglandins); 0  
(Sulfonamides); 0 (rofecoxib); EC 1.14.99.- (cyclooxygenase  
1); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1  
(Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 16 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2001329780 MEDLINE  
DOCUMENT NUMBER: 21290835 PubMed ID: 11397667  
TITLE: Cyclooxygenase-2: a target for the prevention and treatment  
of breast cancer.  
AUTHOR: Howe L R; Subbaramaiah K; Brown A M; Dannenberg A J  
CORPORATE SOURCE: Strang Cancer Research Laboratory, Rockefeller University,  
Box 231, 1230 York Avenue, New York, New York 10021, USA..  
lrhowe@med.cornell.edu  
CONTRACT NUMBER: CA-47207 (NCI)  
CA-89578 (NCI)  
SOURCE: ENDOCRINE-RELATED CANCER, (2001 Jun) 8 (2) 97-114. Ref:  
172  
Journal code: 9436481. ISSN: 1351-0088.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

ABSTRACT:  
Cyclooxygenase-2 (COX-2), an inducible prostaglandin synthase, is normally  
expressed in parts of the kidney and brain. Aberrant COX-2 expression was

first reported in colorectal carcinomas and adenomas, and has now been detected in various human cancers, including those of the breast. Strikingly, COX-2 overexpression in murine mammary gland is sufficient to cause tumour formation. To date, the role of COX-2 in tumorigenesis has been most intensively studied in the colon. Thus, the relationship between COX-2 and neoplasia can best be illustrated with reference to intestinal tumorigenesis. Here we consider the potential utility of selective COX-2 inhibitors for the prevention and treatment of breast cancer. Data for cancers of the colon and breast are compared where possible. In addition, the mechanisms by which COX-2 is upregulated in cancers and contributes to tumorigenesis are discussed. Importantly, several recent studies of mammary tumorigenesis in animal models have found selective COX-2 inhibitors to be effective in the prevention and treatment of breast cancer. Clinical trials will be needed to determine whether COX-2 inhibition represents a useful approach to preventing or treating human breast cancer.

CONTROLLED TERM: Check Tags: Animal; Comparative Study; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

\*Breast Neoplasms: DT, drug therapy

Breast Neoplasms: EN, enzymology

Breast Neoplasms: PC, prevention & control

Colorectal Neoplasms: DT, drug therapy

Colorectal Neoplasms: EN, enzymology

Colorectal Neoplasms: PC, prevention & control

\*Cyclooxygenase Inhibitors: TU, therapeutic use

Gene Expression Regulation, Enzymologic

Gene Expression Regulation, Neoplastic

\*Isoenzymes: AI, antagonists & inhibitors

Isoenzymes: BI, biosynthesis

Isoenzymes: PH, physiology

Prostaglandin-Endoperoxide Synthase: BI, biosynthesis

Prostaglandin-Endoperoxide Synthase: PH, physiology

Sulfonamides: TU, therapeutic use

Up-Regulation

CAS REGISTRY NO.: 169590-42-5 (celecoxib)

CHEMICAL NAME: 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Sulfonamides); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L15 ANSWER 17 OF 17

MEDLINE on STN

ACCESSION NUMBER: 2000131762 MEDLINE

DOCUMENT NUMBER: 20131762 PubMed ID: 10667110

TITLE: [Selective cyclooxygenase-2 (COX-2) inhibitors: importance and limitations].

Inhibiteurs selectifs de la cyclooxygenase de type 2 (COX-2): interets et limites.

AUTHOR: Pairet M; Netter P

CORPORATE SOURCE: Boehringer Ingelheim Pharma KG, Dept of Pulmonary Research, Ingelheim am Rhein, Germany.

SOURCE: THERAPIE, (1999 Jul Aug) 54 (4) 433-45. Ref: 140  
Journal code: 0420544. ISSN: 0040-5957.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

(REVIEW, TUTORIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 20000327

Last Updated on STN: 20000327

Entered Medline: 20000316

ABSTRACT:

The discovery of an inducible form of cyclooxygenase (COX-2) requires a refinement of the theory that inhibition of cyclooxygenase activity explains both therapeutic effects and side-effects of non-steroidal anti-inflammatory drugs (NSAIDs). Selective COX-2 inhibitors have demonstrated in clinical trials a significantly better gastrointestinal tolerability than classical NSAIDs, for the same anti-inflammatory activity. Their tolerability in patients with active ulcer or with a recent history of ulcer as well as in patients suffering from cardiovascular or renal diseases has still to be investigated in detail. Their therapeutic potential in several new indications, including pre-term labour, colorectal cancer and Alzheimer's disease, is currently being investigated.

CONTROLLED TERM: Check Tags: Animal; Human  
 Alzheimer Disease: PC, prevention & control  
 Analgesics: CL, classification  
 Analgesics: PD, pharmacology  
 Anti-Inflammatory Agents, Non-Steroidal: CL, classification  
 Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology  
 Anticarcinogenic Agents: PD, pharmacology  
 Anticarcinogenic Agents: TU, therapeutic use  
 Arachidonic Acids: ME, metabolism  
 Binding Sites: DE, drug effects  
 Clinical Trials  
 Colorectal Neoplasms: PC, prevention & control  
 \*Cyclooxygenase Inhibitors  
 Cyclooxygenase Inhibitors: AE, adverse effects  
 Cyclooxygenase Inhibitors: PD, pharmacology  
 Cyclooxygenase Inhibitors: TU, therapeutic use  
 English Abstract  
 Enzyme Induction: DE, drug effects  
 Gastric Mucosa: DE, drug effects  
 Intestinal Mucosa: DE, drug effects  
 Isoenzymes: BI, biosynthesis  
 Isoenzymes: CH, chemistry  
 \*Isoenzymes: PD, pharmacology  
 Kidney: DE, drug effects  
 Lactones: AE, adverse effects  
 Lactones: PD, pharmacology  
 Lactones: TU, therapeutic use  
 Membrane Lipids: ME, metabolism  
 Mice  
 Peptic Ulcer: CI, chemically induced  
 Phospholipids: ME, metabolism  
 Prostaglandin-Endoperoxide Synthase: BI, biosynthesis  
 Prostaglandin-Endoperoxide Synthase: CH, chemistry  
 \*Prostaglandin-Endoperoxide Synthase: PD, pharmacology  
 Prostaglandins: BI, biosynthesis  
 Reproduction: DE, drug effects  
 Safety  
 Substrate Specificity  
 Sulfonamides: AE, adverse effects  
 Sulfonamides: PD, pharmacology  
 Sulfonamides: TU, therapeutic use  
 Valine: CH, chemistry  
 CAS REGISTRY NO.: 169590-42-5 (celecoxib); 7004-03-7 (Valine)  
 CHEMICAL NAME: 0 (Analgesics); 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Anticarcinogenic Agents); 0 (Arachidonic Acids); 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Lactones); 0 (Membrane Lipids); 0 (Phospholipids); 0 (Prostaglandins); 0 (Sulfonamides); 0 (rofecoxib); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

*intentionally  
blank*

=> fil medl; d que l17; fil embase; d que l52; fil drugu; d que l64  
FILE 'MEDLINE' ENTERED AT 09:55:59 ON 22 OCT 2003

FILE LAST UPDATED: 21 OCT 2003 (20031021/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L6 8161 SEA FILE=MEDLINE ABB=ON CYCLOOXYGENASE INHIBITORS/CT  
L16 2944 SEA FILE=MEDLINE ABB=ON DNA TOPOISOMERASES+NT/CT(L)AI/CT  
L17 1154368 SEA FILE=MEDLINE ABB=ON L6 AND L16

*Antagonists & inhibitors*

FILE 'EMBASE' ENTERED AT 09:56:00 ON 22 OCT 2003  
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FILE COVERS 1974 TO 16 Oct 2003 (20031016/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L20 1180 SEA FILE=EMBASE ABB=ON DNA TOPOISOMERASE INHIBITOR/CT  
L23 3503 SEA FILE=EMBASE ABB=ON IRINOTECAN/CT  
L25 1154368 SEA FILE=EMBASE ABB=ON NEOPLASM+NT/CT  
L26 30090 SEA FILE=EMBASE ABB=ON ANTINEOPLASTIC ACTIVITY+NT/CT  
L27 80280 SEA FILE=EMBASE ABB=ON CANCER CHEMOTHERAPY/CT  
L31 28382 SEA FILE=EMBASE ABB=ON DRUG POTENTIATION/CT  
L32 27860 SEA FILE=EMBASE ABB=ON CANCER COMBINATION CHEMOTHERAPY/CT  
L47 4014 SEA FILE=EMBASE ABB=ON CYCLOOXYGENASE 2 INHIBITOR/CT  
L48 2529 SEA FILE=EMBASE ABB=ON CELECOXIB/CT  
L49 27 SEA FILE=EMBASE ABB=ON (L20 OR L23) (L)CB/CT AND (L47 OR L48) (L)CB/CT  
L50 17 SEA FILE=EMBASE ABB=ON (L32 OR L26 OR L27) AND L49  
L51 5 SEA FILE=EMBASE ABB=ON L49 AND L25 AND L31  
L52 1154368 SEA FILE=EMBASE ABB=ON L50 OR L51

*CB = drug combination*

FILE 'DRUGU' ENTERED AT 09:56:00 ON 22 OCT 2003  
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FILE LAST UPDATED: 16 OCT 2003 <20031016/UP>  
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001. <<<  
>>> (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION <<<  
>>> SEE HELP COST <<<

>>> FILE COVERS 1983 TO DATE <<<  
>>> THESAURUS AVAILABLE IN /CT <<<

L58 1005 SEA FILE=DRUGU ABB=ON CELECOXIB/CT  
L59 3358 SEA FILE=DRUGU ABB=ON CYCLOOXYGENASE-2-INHIBITOR#/CT  
L60 1858 SEA FILE=DRUGU ABB=ON IRINOTECAN/CT  
L61 2674 SEA FILE=DRUGU ABB=ON TOPOISOMERASE-I-INHIBITOR#/CT  
L63 111712 SEA FILE=DRUGU ABB=ON COMB./CT  
L64 6 SEA FILE=DRUGU ABB=ON (L58 OR L59) AND (L60 OR L61) AND L63

=> dup rem 117,164,152  
FILE 'MEDLINE' ENTERED AT 09:56:05 ON 22 OCT 2003

FILE 'DRUGU' ENTERED AT 09:56:05 ON 22 OCT 2003  
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FILE 'EMBASE' ENTERED AT 09:56:05 ON 22 OCT 2003  
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PROCESSING COMPLETED FOR L17  
PROCESSING COMPLETED FOR L64  
PROCESSING COMPLETED FOR L52

L65 26 DUP REM L17 L64 L52 (2 DUPLICATES REMOVED)  
ANSWERS '1-3' FROM FILE MEDLINE  
ANSWERS '4-9' FROM FILE DRUGU  
ANSWERS '10-26' FROM FILE EMBASE

=> d iall 1-26; fil hom

L65 ANSWER 1 OF 26 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2003133447 MEDLINE  
DOCUMENT NUMBER: 22534473 PubMed ID: 12647986  
TITLE: Systemic therapy for advanced pancreatic cancer.  
AUTHOR: El-Rayes Basil F; Philip Philip A  
CORPORATE SOURCE: Division of Haematology and Oncology, Karmanos Cancer  
Institute, Wayne State University, Detroit, MI 48201, USA.  
SOURCE: Expert Rev Anticancer Ther, (2002 Aug) 2 (4) 426-36. Ref:  
78  
Journal code: 101123358. ISSN: 1473-7140.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200304  
ENTRY DATE: Entered STN: 20030322  
Last Updated on STN: 20030430  
Entered Medline: 20030429

ABSTRACT:

Death from pancreatic cancer remains high with few long-term survivors. Systemic chemotherapy with 5-fluorouracil-based combinations had minimal impact on natural history of this disease. Several new agents with activity against pancreatic cancer have been identified over the past decade. Gemcitabine has modest activity in this disease. Combination chemotherapy trials incorporating gemcitabine, cisplatin, 5-fluorouracil, oxaliplatin, docetaxel or irinotecan show improved outcomes in objective response rates and survival that need to be confirmed in prospectively randomized studies. Advancement in the understanding of the biology of pancreatic cancer has helped identify several molecular targets for the development of novel therapies. Ongoing and future treatment regimens for pancreatic cancer will incorporate traditional cytotoxic drugs and novel targeted therapies.

CONTROLLED TERM: Check Tags: Human  
Angiogenesis Inhibitors: TU, therapeutic use

Antimetabolites, Antineoplastic: TU, therapeutic use

\*Antineoplastic Agents: TU, therapeutic use

Cell Cycle: DE, drug effects

**Cyclooxygenase Inhibitors: TU, therapeutic use**

**DNA Topoisomerases, Type I: AI, antagonists & inhibitors**

\*Deoxycytidine: AA, analogs & derivatives

Deoxycytidine: TU, therapeutic use

Drug Therapy, Combination

Enzyme Inhibitors: TU, therapeutic use

Fluorouracil: TU, therapeutic use

Genes, ras: DE, drug effects

Isoenzymes: ME, metabolism

Pancreatic Neoplasms: DT, drug therapy

\*Pancreatic Neoplasms: TH, therapy

Prostaglandin-Endoperoxide Synthase: ME, metabolism

Signal Transduction: DE, drug effects

CAS REGISTRY NO.: 103882-84-4 (gemcitabine); 51-21-8 (Fluorouracil); 951-77-9 (Deoxycytidine)

CHEMICAL NAME: 0 (Angiogenesis Inhibitors); 0 (Antimetabolites, Antineoplastic); 0 (Antineoplastic Agents); 0 (Cyclooxygenase Inhibitors); 0 (Enzyme Inhibitors); 0 (Isoenzymes); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase); EC 5.99.1.2 (DNA Topoisomerases, Type I)

L65 ANSWER 2 OF 26

MEDLINE on STN

ACCESSION NUMBER: 2003224150 MEDLINE

DOCUMENT NUMBER: 22630717 PubMed ID: 12745645

TITLE: Cancer therapy: new targets for chemotherapy.

AUTHOR: Novotny Ladislav; Szekeres Thomas

CORPORATE SOURCE: Kuwait University, Faculty of Pharmacy, Department of Chemistry, Kuwait, Kuwait.. novotny@hsc.kuniv.edu.kw

SOURCE: Hematology, (2003 Jun) 8 (3) 129-37. Ref: 63

Journal code: 9708388. ISSN: 1024-5332.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200309

ENTRY DATE: Entered STN: 20030515

Last Updated on STN: 20030903

Entered Medline: 20030902

#### ABSTRACT:

The number two cause of mortality in developed countries is cancer. Despite the enormous effort put into cancer prevention, early diagnosis and treatment, it is likely that the incidence of the cancer morbidity and mortality will increase for the foreseeable future. This is due to various factors such as increased life expectancy, changes in environment and also the socio-economic situation around the world. Some cancer attracts more attention than others and increasingly epidemiological information is reaching the general public and is beginning to influence behavior. It is now well recognized that, for example, 1 of 8 women in the industrialized world will be diagnosed with breast cancer. Additionally, a strong correlation was established between lung cancer incidence and smoking and it is broadly accepted that the incidence of colon cancer is directly related to age and diet, and has been increasing over time. The current failure of preventive measures to significantly reduce the increasing incidence of these common tumors illustrates the importance of effective cancer treatment strategies, including chemotherapy. The combination of various anticancer drugs, given together with surgery and radiotherapy, gives hope to many patients. There has been recent evidence of improved

therapeutic outcome with recent approaches and newer agents but for continuing effective chemotherapeutic treatment there is a need for a detailed understanding of their mechanisms of action and on the rationale of their application. This review attempts to provide up-to-date information regarding the development of new and innovative treatment strategies for cancer chemotherapy. Virtually, every year several of new targets for cancer therapy on both, cellular and molecular levels, are identified and new drugs enter not only clinical trials but also are included in well accepted and documented therapeutic protocols. As this review is in addition to our review published previously (Medical Principles and Practice 11, 2002, 117-125), we have tried to include new and innovative targets and drugs that attract attention at present. Although it is not possible to provide a complete list of all achievements and cover all work done in this field, we hope to be able to give some insight into this rapidly developing area.

CONTROLLED TERM: Check Tags: Human  
 Alkyl and Aryl Transferases: AI, antagonists & inhibitors  
 Antigens, Neoplasm: IM, immunology  
 Antineoplastic Agents: CL, classification  
 \*Antineoplastic Agents: PD, pharmacology  
 Antineoplastic Agents: TU, therapeutic use  
 Apoptosis: DE, drug effects  
 Cyclin-Dependent Kinases: AI, antagonists & inhibitors  
 Cyclooxygenase Inhibitors: PD, pharmacology  
 Cysteine Proteinase Inhibitors: PD, pharmacology  
 Cysteine Proteinase Inhibitors: TU, therapeutic use  
 DNA Methylation: DE, drug effects  
 DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
 DNA Topoisomerases, Type II: AI, antagonists & inhibitors  
 Drug Design  
 Enzyme Inhibitors: PD, pharmacology  
 Enzyme Inhibitors: TU, therapeutic use  
 Membrane Glycoproteins: TU, therapeutic use  
 Neoplasm Proteins: AI, antagonists & inhibitors  
 \*Neoplasms: DT, drug therapy  
 Telomerase: AI, antagonists & inhibitors  
 Tumor Necrosis Factor: TU, therapeutic use

CHEMICAL NAME: 0 (Antigens, Neoplasm); 0 (Antineoplastic Agents); 0 (Cyclooxygenase Inhibitors); 0 (Cysteine Proteinase Inhibitors); 0 (Enzyme Inhibitors); 0 (Membrane Glycoproteins); 0 (Neoplasm Proteins); 0 (TNF-related apoptosis-inducing ligand); 0 (Tumor Necrosis Factor); EC 2.5 (Alkyl and Aryl Transferases); EC 2.5.1.29 (farnesyltranstransferase); EC 2.7.1.37 (Cyclin-Dependent Kinases); EC 2.7.7.- (Telomerase); EC 5.99.1.2 (DNA Topoisomerases, Type I); EC 5.99.1.3 (DNA Topoisomerases, Type II)

L65 ANSWER 3 OF 26 MEDLINE on STN  
 ACCESSION NUMBER: 2003036575 MEDLINE  
 DOCUMENT NUMBER: 22431836 PubMed ID: 12542978  
 TITLE: Current mechanistic approaches to the chemoprevention of cancer.  
 AUTHOR: Steele Vernon E  
 CORPORATE SOURCE: Chemoprevention Agent Development Research Group, Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA..  
 vsly@nih.gov  
 SOURCE: J Biochem Mol Biol, (2003 Jan 31) 36 (1) 78-81. Ref: 27  
 Journal code: 9702084. ISSN: 1225-8687.  
 PUB. COUNTRY: Korea (South)  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200306  
ENTRY DATE: Entered STN: 20030125  
Last Updated on STN: 20030621  
Entered Medline: 20030620

## ABSTRACT:

The prevention of cancer is one of the most important public health and medical practices of the 21st century. We have made much progress in this new emerging field, but so much remains to be accomplished before widespread use and practice become common place. Cancer chemoprevention encompasses the concepts of inhibition, reversal, and retardation of the cancer process. This process, called carcinogenesis, requires 20-40 years to reach the endpoint called invasive cancer. It typically follows multiple, diverse and complex pathways in a stochastic process of clonal evolution. These pathways appear amenable to inhibition, reversal or retardation at various points. We must therefore identify key pathways in the evolution of the cancer cell that can be exploited to prevent this carcinogenesis process. Basic research is identifying many genetic lesions and epigenetic processes associated with the progression of precancer to invasive disease. Many of these early precancerous lesions favor cell division over quiescence and protect cells against apoptosis when signals are present. Many oncogenes are active during early development and are reactivated in adulthood by aberrant gene promoting errors. Normal regulatory genes are mutated, making them insensitive to normal regulatory signals. Tumor suppressor genes are deleted or mutated rendering them inactive. Thus there is a wide range of defects in cellular machinery which can lead to evolution of the cancer phenotype. Mistakes may not have to appear in a certain order for cells to progress along the cancer pathway. To conquer this diverse disease, we must attack multiple key pathways at once for a predetermined period of time. Thus, agent combination prevention strategies are essential to decrease cancer morbidity. Furthermore, each cancer type may require custom combination of prevention strategies to be successful.

CONTROLLED TERM: Check Tags: Animal; Human  
\*Antioxidants: PD, pharmacology  
Cell Division: PH, physiology  
Chemoprevention  
\*Cyclooxygenase Inhibitors: PD, pharmacology  
DNA Methylation: DE, drug effects  
DNA Topoisomerases, Type I: AI, antagonists & inhibitors  
Enzyme Inhibitors: PD, pharmacology  
Gene Expression Regulation, Neoplastic  
Inflammation: ME, metabolism  
Neoplasms: GE, genetics  
Neoplasms: ME, metabolism  
\*Neoplasms: PC, prevention & control  
Oncogenes  
Prostaglandin-Endoperoxide Synthase: ME, metabolism  
\*Selective Estrogen Receptor Modulators: PD, pharmacology  
0 (Antioxidants); 0 (Cyclooxygenase Inhibitors); 0 (Enzyme Inhibitors); 0 (Selective Estrogen Receptor Modulators); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase); EC 5.99.1.2 (DNA Topoisomerases, Type I)

## CHEMICAL NAME:

L65 ANSWER 4 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1  
ACCESSION NUMBER: 2002-49624 DRUGU P S E  
TITLE: Cyclooxygenase-2 inhibition with celecoxib enhances antitumor efficacy and reduces diarrhea side effect of CPT-11.  
AUTHOR: Trifan O C; Durham W F; Salazar V S; Horton J; Levine B D; Zweifel B S; Davis T W; Masferrer J L  
CORPORATE SOURCE: Pharmacia

LOCATION: Chesterfield, Mo., USA  
SOURCE: Cancer Res. (62, No. 20, 5778-84, 2002) 3 Fig. 3 Tab. 55 Ref.  
CODEN: CNREA8 ISSN: 0008-5472  
AVAIL. OF DOC.: Oncology Pharmacology, AA5C, Pharmacia Corp., 700  
Chesterfield Parkway North, Chesterfield, MO 63198, U.S.A.  
(e-mail: ovidiu.c.trifan@pharmacia.com).  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

P.o. celecoxib (CEL) enhanced the antitumor effect of i.p. CPT-11 (irinotecan; both Pharmacia) in mice harboring HT-29 and colon-26 tumors. CEL and CPT-11 prevented the tumor-induced body weight loss. I.v. CPT-11 induced diarrhea, an effect that was prevented by s.c. atropine pretreatment. CEL dose-dependently reduced diarrhea. CPT-11 increased COX-2 protein and PGE2 levels in rat colon. CEL restored the PGE2 levels. S.c. anti-PGE2 Ab also reduced CPT-11-induced diarrhea. P.o. indometacin and SC-560 reduced tissue TXB2, whereas CEL and CPT-11 had no effect on TXB2 content in the colon. These findings suggest that combining CEL with CPT-11 may be beneficial in the improvement of the outcome of treatment in cancer patients.

SECTION HEADING: P Pharmacology  
S Adverse Effects  
E Endocrinology

CLASSIF. CODE: 16 Gastrointestinal  
34 Toxicology  
43 Analgesics, NSAIDs  
52 Chemotherapy - non-clinical

## CONTROLLED TERM:

HT29 \*OC; COLON \*OC; INTESTINE \*OC; GASTROENTEROPATHY \*OC;  
CARCINOMA \*OC; WEIGHT-LOSS \*AE; ANIMAL-NEOPLASM \*OC;  
BODY-WEIGHT \*AE; INDOMETACIN \*RC; SC-560 \*RC; ATROPINE \*RC;  
MOUSE \*FT; RAT \*FT; IN-VIVO \*FT; ALONE \*FT; COMB.  
\*FT; BODY-WEIGHT \*FT; BLOOD-PLASMA \*FT; CONC. \*FT; PGE2 \*FT;  
COLON \*FT; INTESTINE \*FT; THROMBOXANE-A2 \*FT; THROMBOXANE-B2  
\*FT; TOX. \*FT; CYTOSTATIC \*FT; LAB.ANIMAL \*FT  
[01] CELECOXIB \*PH; CELECOXIB \*AE; PHARMACIA  
\*FT; DR9605582 \*RN; P.O. \*FT; CYCLOOXYGENASE-2-INHIBITOR  
\*FT; ANTIDIARRHEIC \*FT; CYCLOOXYGENASE-INHIBITOR \*FT;  
PROSTAGLANDIN-ANTAGONIST \*FT; ANALGESICS \*FT;  
ANTIINFLAMMATORIES \*FT; ANTIRHEUMATICS \*FT;  
CYCLOOXYGENASE-2-INHIBITORS \*FT; PROSTAGLANDIN-  
ANTAGONISTS \*FT; CYCLOOXYGENASE-INHIBITORS \*FT; PH \*FT; AE  
\*FT

CAS REGISTRY NO.: 169590-42-5

[02]

IRINOTECAN \*PH; IRINOTECAN \*AE; PHARMACIA  
\*FT; DIARRHEA \*AE; GASTROENTEROPATHY \*AE; CPT-11 \*RN; I.P.  
\*FT; INJECTION \*FT; CYTOSTATICS \*FT; TOPOISOMERASE-I-  
INHIBITORS \*FT; TOPOISOMERASE-INHIBITORS \*FT; PH \*FT; AE  
\*FT

CAS REGISTRY NO.: 97682-44-5

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L65 ANSWER 5 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-23410 DRUGU P B

TITLE: Effect of non-steroidal anti-inflammatory drugs on colon  
carcinoma Caco-2 cells responsiveness to topoisomerase  
inhibitor drugs.

AUTHOR: Ricchi P; Matola T D; Ruggiero G; Zanzi D; Apicella A; di

CORPORATE SOURCE: Palma A; Pensabene M; Pignata S; Zarrilli R; Acquaviva A M  
LOCATION: Univ.Naples-Federico-II  
SOURCE: Naples, It.  
Br.J.Cancer (86, No. 9, 1501-09, 2002) 6 Fig. 2 Tab. 54 Ref.  
CODEN: BJCAAI ISSN: 0007-0920  
AVAIL. OF DOC.: Dipartimento di Biologia e Patologia Cellulare e Molecolare,  
Facolta di Medicina e Chirurgia, Universita 'Federico II',  
via S. Pansini 5, 80131 Napoli, Italy. (A.M.A.). (e-mail:  
angacqua@unina.it).  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

Aspirin (Sigma-Chem.) dose-dependently decreased both etoposide (VP-16, Bristol-Squibb)- and irinotecan (CPT-11, Rhone-Poulenc-Rorer)-induced apoptosis and increased cell viability in human colon Caco-2 cancer cells. NS-398 also decreased VP-16- and CPT-11-dependent apoptosis. Aspirin dose-dependently increased bcl-2 levels, while NS-398 decreased the levels of bcl-2. Results suggest that aspirin, but not NS-398, determines a cell cycle arrest associated with death suppression. This provides a plausible mechanism for the inhibition of apoptosis and increase in survival observed in anticancer drug and aspirin co-treatment.

SECTION HEADING: P Pharmacology  
B Biochemistry

CLASSIF. CODE: 27 Molecular Biology  
43 Analgesics, NSAIDs  
52 Chemotherapy - non-clinical  
73 Trial Preparations

## CONTROLLED TERM:

[01] COMB. \*FT; IN-VITRO \*FT; CACO2-CELL \*FT;  
ADENOCARCINOMA \*FT; TUMOR-CELL \*FT; TISSUE-CULTURE \*FT  
ASPIRIN \*PH; SIGMA-CHEM. \*FT; ASPIRIN \*RN; BCL-2 \*FT;  
APOPTOSIS-INHIBITOR \*FT; MODE-OF-ACT. \*FT; ANALGESICS \*FT;  
ANTIPYRETICS \*FT; ANTIRHEUMATICS \*FT; ANTIAGGREGANTS \*FT;  
ANTIINFLAMMATORIES \*FT; PH \*FT  
CAS REGISTRY NO.: 50-78-2  
[02] NS-398 \*PH; NS-398 \*RN; BCL-2 \*FT; APOPTOSIS-INHIBITOR \*FT;  
MODE-OF-ACT. \*FT; TRIAL-PREP. \*FT; ANTIINFLAMMATORIES \*FT;  
ANALGESICS \*FT; ANTIPYRETICS \*FT; CYCLOOXYGENASE-2-  
INHIBITORS \*FT; PH \*FT  
[03] ETOPOSIDE \*PH; BRISTOL-SQUIBB \*FT; ETOPOSIDE \*RN; CYTOSTATICS  
\*FT; TOPOISOMERASE-INHIBITORS \*FT; PH \*FT  
CAS REGISTRY NO.: 33419-42-0  
[04] IRINOTECAN \*PH; RHONE-POULENC-RORER \*FT; CPT-11  
\*RN; CYTOSTATICS \*FT; TOPOISOMERASE-I-INHIBITORS  
\*FT; TOPOISOMERASE-INHIBITORS \*FT; PH \*FT  
CAS REGISTRY NO.: 97682-44-5  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

L65 ANSWER 6 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 2002-50056 DRUGU T S  
TITLE: Phase I studies using capecitabine combined with conformal  
radiation therapy (RT), paclitaxel, CPT-11 and celecoxib in  
gastrointestinal malignancies.  
AUTHOR: Kennedy A S; Van Echo D A; Volpe C; Moesinger R; Shibata D;  
Darwin P; Haluszka O  
CORPORATE SOURCE: Univ.Maryland  
LOCATION: Baltimore, Md., USA

SOURCE: ; Proc.Am.Soc.Clin.Oncol. (21, Pt. 2, 300b, 2002)  
CODEN: ; 7790  
AVAIL. OF DOC.: University of Maryland Greenebaum Cancer Center, Baltimore,  
MD, U.S.A.  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

Phase I studies were performed in 27 patients combining p.o. capecitabine (C) with i.v. infused paclitaxel (P) + radiotherapy (RT) in upper GI cancer (pancreas, bile duct, gallbladder) or C with i.v. infused CPT-11 (irinotecan) + RT in rectal cancer. The results showed that C + RT and other chemotherapy agents was a promising and safe approach for GI malignancies. Treatment related enteritis was seen. The MTD of C was 1500 mg p.o. b.i.d. given on RT days with wkly P for pancreas and biliary tree malignancies. The MTD of C + pelvic RT and wkly CPT-11 for rectal cancer was not achieved. Further patients will be studied using C at the MTD and celecoxib from the start of RT. (conference abstract: 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida, USA, 2002).

SECTION HEADING: T Therapeutics  
S Adverse Effects

CLASSIF. CODE: 35 Adverse Reactions  
51 Chemotherapy - clinical  
64 Clinical Trials

## CONTROLLED TERM:

RECTUM \*TR; PANCREAS \*TR; BILIARY-TRACT-DISEASE \*TR;  
GASTROENTEROPATHY \*TR; PANCREOPATHY \*TR; CHOLANGIOCARCINOMA  
\*TR; ENTERITIS \*AE; NEOPLASM \*TR; GASTROENTEROPATHY \*AE;  
**CELECOXIB** \*RC; IN-VIVO \*FT; CASES \*FT; PHASE-I \*FT;  
RADIOTHERAPY \*FT; **COMB.** \*FT; CYTOSTATIC \*FT;  
CLIN.TRIAL \*FT

[01] CAPECITABINE \*TR; CAPECITABINE \*AE; DR9504617 \*RN; P.O. \*FT;  
CYTOSTATICS \*FT; SYNERGISTS \*FT; TR \*FT; AE \*FT

CAS REGISTRY NO.: 154361-50-9

[02] PACLITAXEL \*TR; PACLITAXEL \*AE; TAXOL \*RN; I.V. \*FT; INFUSION  
\*FT; INJECTION \*FT; CYTOSTATICS \*FT; P-GLYCOPROTEIN-  
INHIBITORS \*FT; TR \*FT; AE \*FT

CAS REGISTRY NO.: 33069-62-4

[03] **IRINOTECAN** \*TR; **IRINOTECAN** \*AE; CPT-11  
\*RN; I.V. \*FT; INFUSION \*FT; CYTOSTATICS \*FT;  
**TOPOISOMERASE-I-INHIBITORS** \*FT; TOPOISOMERASE-  
INHIBITORS \*FT; TR \*FT; AE \*FT

CAS REGISTRY NO.: 97682-44-5

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L65 ANSWER 7 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-44843 DRUGU T S V

TITLE: A phase II trial of celecoxib (CX), irinotecan (I),  
5-fluorouracil (5FU) and leucovorin (LCV) in patients (pts)  
with unresectable or metastatic colorectal cancer (CRC).

AUTHOR: Blanke C D; Benson A B; Dragovich T; Lenz H J; Haller D;  
Robles C; Buchbinder A

CORPORATE SOURCE: Univ.Oregon-Health+Sci.; Univ.Northwestern;  
Arizona-Cancer-Cent.; Univ.Southern-California

LOCATION: Portland, Oreg.; Chicago, Ill.; Tucson, Ariz.; Los Angeles,  
Cal.; Philadelphia, Pa.; USA

SOURCE: ; Proc.Am.Soc.Clin.Oncol. (21, Pt. 1, 127a, 2002)  
CODEN: ; 7790

AVAIL. OF DOC.: Oregon Health + Science University, Portland, OR, U.S.A.  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

A Phase II trial of p.o. celecoxib, irinotecan, fluorouracil and leucovorin in 23 patients with unresectable or metastatic colorectal cancer is reported. Hematologic toxicity was modest. Other side-effects were mainly GI symptoms with some cardiovascular toxicity. The combination was active with less neutropenia than expected from chemotherapy alone. Prophylactic aspirin is recommended. (conference abstract: 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida, USA, 2002).

SECTION HEADING: T Therapeutics  
S Adverse Effects  
V Vitamins

CLASSIF. CODE: 35 Adverse Reactions  
42 Vitamins  
51 Chemotherapy - clinical  
64 Clinical Trials

## CONTROLLED TERM:

METASTATIC \*TR; COLON \*TR; RECTUM \*TR; INTESTINE \*TR;  
GASTROENTEROPATHY \*TR; NEOPLASM \*TR; NEUTROPENIA \*AE;  
DIARRHEA \*AE; NAUSEA \*AE; MYOCARD.INFARCT. \*AE; APOPLEXY \*AE;  
MARROW-DISEASE \*AE; GASTROENTEROPATHY \*AE; CARDIOPATHY \*AE;  
CORONARY-DISEASE \*AE; CEREBROVASCULAR-DISEASE \*AE; CASES \*FT;  
IN-VIVO \*FT; PHASE-II \*FT; CYTOSTATIC \*FT; CYTOSTATIC-COMB.  
\*FT; CLIN.TRIAL \*FT; COMB. \*FT

[01]

**CELECOXIB** \*TR; **CELECOXIB** \*AE; DR9605582  
\*RN; P.O. \*FT; ANALGESICS \*FT; ANTIINFLAMMATORIES \*FT;  
ANTIRHEUMATICS \*FT; **CYCLOOXYGENASE-2-INHIBITORS**  
\*FT; PROSTAGLANDIN-ANTAGONISTS \*FT; TR \*FT; AE \*FT

CAS REGISTRY NO.: 169590-42-5

[02]

FLUOROURACIL \*TR; FLUOROURACIL \*AE; FLUOROURA \*RN;  
CYTOSTATICS \*FT; THYMIDYLATE-SYNTHASE-INHIBITORS \*FT; TR \*FT;  
AE \*FT

CAS REGISTRY NO.: 51-21-8

[03]

**IRINOTECAN** \*TR; **IRINOTECAN** \*AE; CPT-11  
\*RN; CYTOSTATICS \*FT; **TOPOISOMERASE-I-INHIBITORS**  
\*FT; TOPOISOMERASE-INHIBITORS \*FT; TR \*FT; AE \*FT

CAS REGISTRY NO.: 97682-44-5

[04]

FOLINATE CALCIUM \*TR; FOLINATE CALCIUM \*AE; FOLINACA \*RN;  
VITAMINS-B \*FT; THYMIDYLATE-SYNTHASE-INHIBITORS \*FT; TR \*FT;  
AE \*FT

CAS REGISTRY NO.: 1492-18-8

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L65 ANSWER 8 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-48871 DRUGU T V S

TITLE: A phase II trial of irinotecan (I), 5-fluorouracil (F),  
leucovorin (L) (IFL), celecoxib and glutamine as first line  
therapy for advanced colorectal cancer: a Hoosier Oncology  
Group study.

AUTHOR: Sweeney C; Seitz D; Ansari R; Chowhan N; Pletcher W; Vinson  
J; Stoner C; Sawi J; Loehrer P J

CORPORATE SOURCE: Univ.Indiana

LOCATION: Indianapolis, South Bend, New Albany; Elkhart, Ind., USA

SOURCE: ; Proc.Am.Soc.Clin.Oncol. (21, Pt. 2, 105b, 2002)

CODEN: ; 7790

AVAIL. OF DOC.: Indiana University, Indianapolis, IN, U.S.A.  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

This phase II trial evaluated the IFL infusional combination, of irinotecan (I), 5-fluorouracil (F) and leucovorin (L), plus p.o. celecoxib and glutamine (as prophylaxis of chemotherapy-induced diarrhea), as first line therapy for advanced colorectal cancer in 23 patients. The overall response rate was 31%. Despite the co-administration of celecoxib and glutamine, the diarrhea associated with IFL remained a problem. However, the absence of grade 4 diarrhea, neutropenic fevers and the lower rate of grade 3/4 myelosuppression make this combination worthy of further evaluation. (conference abstract: 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida, USA, 2002).

SECTION HEADING: T Therapeutics  
V Vitamins  
S Adverse Effects

CLASSIF. CODE: 16 Gastrointestinal  
35 Adverse Reactions  
42 Vitamins  
51 Chemotherapy - clinical  
64 Clinical Trials

## CONTROLLED TERM:

[01] CASES \*FT; IN-VIVO \*FT; PHASE-II \*FT; PROGNOSIS \*FT;  
COMB. \*FT; CLIN.TRIAL \*FT  
CELECOXIB \*TR; DIARRHEA \*TR; GASTROENTEROPATHY \*TR;  
DR9605582 \*RN; ANTIDIARRHEIC \*FT; P.O. \*FT; PROPHYLAXIS \*FT;  
ANALGESICS \*FT; ANTIINFLAMMATORIES \*FT; ANTIRHEUMATICS \*FT;  
CYCLOOXYGENASE-2-INHIBITORS \*FT; PROSTAGLANDIN-  
ANTAGONISTS \*FT; CYCLOOXYGENASE-INHIBITORS \*FT; TR \*FT

CAS REGISTRY NO.: 169590-42-5  
[02] GLUTAMINE \*TR; DIARRHEA \*TR; GASTROENTEROPATHY \*TR; GLUTAMINE  
\*RN; ANTIDIARRHEIC \*FT; P.O. \*FT; PROPHYLAXIS \*FT; TR \*FT

[03] IRINOTECAN \*TR; IRINOTECAN \*AE; ADVANCED  
\*TR; COLORECTAL \*TR; COLON \*TR; RECTUM \*TR; GASTROENTEROPATHY  
\*TR; NEOPLASM \*TR; DIARRHEA \*AE; AGRANULOCYTOSIS \*AE;  
DEHYDRATION \*AE; VEIN \*AE; THROMBOSIS \*AE; GASTROENTEROPATHY  
\*AE; MARROW-DISEASE \*AE; CPT-11 \*RN; CYTOSTATIC-COMB. \*FT;  
PARENTERAL \*FT; INFUSION \*FT; CYTOSTATIC \*FT; COMB.  
\*FT; INJECTION \*FT; CYTOSTATICS \*FT; TOPOISOMERASE-I-  
INHIBITORS \*FT; TOPOISOMERASE-INHIBITORS \*FT; TR \*FT; AE  
\*FT

CAS REGISTRY NO.: 97682-44-5  
[04] FLUOROURACIL \*TR; FLUOROURACIL \*AE; ADVANCED \*TR; COLORECTAL  
\*TR; COLON \*TR; RECTUM \*TR; GASTROENTEROPATHY \*TR; NEOPLASM  
\*TR; DIARRHEA \*AE; AGRANULOCYTOSIS \*AE; DEHYDRATION \*AE; VEIN  
\*AE; THROMBOSIS \*AE; GASTROENTEROPATHY \*AE; MARROW-DISEASE  
\*AE; FLUOROURA \*RN; CYTOSTATIC-COMB. \*FT; PARENTERAL \*FT;  
INFUSION \*FT; CYTOSTATIC \*FT; COMB. \*FT; INJECTION  
\*FT; CYTOSTATICS \*FT; THYMIDYLATE-SYNTHASE-INHIBITORS \*FT; TR  
\*FT; AE \*FT

CAS REGISTRY NO.: 51-21-8  
[05] FOLINATE CALCIUM \*TR; FOLINATE CALCIUM \*AE; ADVANCED \*TR;  
COLORECTAL \*TR; COLON \*TR; RECTUM \*TR; GASTROENTEROPATHY \*TR;  
NEOPLASM \*TR; DIARRHEA \*AE; AGRANULOCYTOSIS \*AE; DEHYDRATION  
\*AE; VEIN \*AE; THROMBOSIS \*AE; GASTROENTEROPATHY \*AE;  
MARROW-DISEASE \*AE; FOLINACA \*RN; CYTOSTATIC-COMB. \*FT;  
PARENTERAL \*FT; INFUSION \*FT; COMB. \*FT; INJECTION

\*FT; VITAMINS-B \*FT; THYMIDYLATE-SYNTHASE-INHIBITORS \*FT; TR  
\*FT; AE \*FT

CAS REGISTRY NO.: 1492-18-8  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

L65 ANSWER 9 OF 26 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 2002-25976 DRUGU P  
TITLE: Cyclooxygenase-2 (Cox-2) inhibition attenuates the growth and  
metastatic potential of colorectal carcinoma (CRC) in mice.  
AUTHOR: Yao M; Lam E C; Kelly C R; Luk P; Kwong E C; Kargman S; Evans  
J F; Wolfe M M  
LOCATION: Boston, Mass; West Point, Pa., USA; Montreal, Que., Can.  
SOURCE: Gastroenterology (122, No. 4, Suppl., A4, 2002)  
CODEN: GASTAB ISSN: 0016-5085  
AVAIL. OF DOC.: No reprint address.  
LANGUAGE: English  
DOCUMENT TYPE: Journal

## ABSTRACT:

It was determined whether p.o. rofecoxib, a specific cyclooxygenase-2 (COX-2) inhibitor, could reduce tumor growth and metastatic potential of colorectal carcinoma (CRC) (MC-26 cells) in-vivo in mice. The results showed that COX-2 inhibition with rofecoxib decreased the growth and liver metastatic potential of CRC in mice. COX-2 inhibition also augmented the antineoplastic properties of standard cytostatics, 5-fluorouracil (5-FU) plus leucovorin (LV, folinate calcium) and CPT-11 (irinotecan). It was concluded that the specific COX-2 inhibitor rofecoxib may have therapeutic benefit in metastatic CRC. (conference abstract: 103rd Annual Meeting of the American Gastroenterological Association, San Francisco, California, USA, 2002).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 52 Chemotherapy - non-clinical

## CONTROLLED TERM:

CARCINOMA \*OC; MC-26 \*OC; ANIMAL-NEOPLASM \*OC; IN-VIVO \*FT;  
MOUSE \*FT; **COMB.** \*FT; CYTOSTATIC \*FT; LAB.ANIMAL  
\*FT

[01] ROFECOXIB \*PH; DR9607965 \*RN; ALONE \*FT; P.O. \*FT;  
**CYCLOOXYGENASE-2-INHIBITORS** \*FT; PROSTAGLANDIN-  
ANTAGONISTS \*FT; ANALGESICS \*FT; ANTIINFLAMMATORIES \*FT; PH  
\*FT

[02] FLUOROURACIL \*PH; FOLINATE-CALCIUM \*RC; FLUOROURA \*RN;  
CYTOSTATICS \*FT; THYMIDYLATE-SYNTHASE-INHIBITORS \*FT; PH \*FT

CAS REGISTRY NO.: 51-21-8

[03] **IRINOTECAN** \*PH; CPT-11 \*RN; CYTOSTATICS \*FT;  
**TOPOISOMERASE-I-INHIBITORS** \*FT; TOPOISOMERASE-  
INHIBITORS \*FT; PH \*FT

CAS REGISTRY NO.: 97682-44-5  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

L65 ANSWER 10 OF 26 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003120764 EMBASE  
TITLE: Recent advances in the pharmacological treatment of  
colorectal cancer.  
AUTHOR: Messersmith W.; Laheru D.; Hidalgo M.  
CORPORATE SOURCE: Dr. M. Hidalgo, Sydney Kimmel Comprehen. Can. Ctr., 1650  
Orleans Street, Baltimore, MD 21231-1000, United States.  
mhidalgl@jhmi.edu

SOURCE: Expert Opinion on Investigational Drugs, (1 Mar 2003) 12/3 (423-434).

Refs: 97

ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Recent advances in the treatment of colorectal cancer have lead to significant gains in response rates and survival. The combination of newer agents such as irinotecan and oxaliplatin with 5-fluorouracil/leucovorin using various dosing schedules in the metastatic setting has resulted in a steady improvement in the outcome of patients with colorectal cancer. Experimental therapies such as epidermal growth factor receptor inhibitors, vascular endothelial growth factor inhibitors and cyclooxygenase-2 inhibitors, have shown promise in early clinical trials and have acceptable toxicity profiles. Efforts towards improving risk-stratification of stage II colorectal cancer patients and optimising therapy in patients with advanced disease, have focused on molecular and genetic markers. It is hoped that the addition of new therapies to existing drug combinations, as well as further advances in the understanding of colorectal cancer biology, will lead to further improvement in survival and quality of life for patients.

CONTROLLED TERM: Medical Descriptors:

- \*colorectal cancer: DI, diagnosis
- \*colorectal cancer: DT, drug therapy
- \*colorectal cancer: RT, radiotherapy
- \*colorectal cancer: SU, surgery
- treatment planning
- cancer survival
- metastasis: DT, drug therapy
- treatment outcome
- risk assessment
- cancer staging
- advanced cancer: DI, diagnosis
- advanced cancer: DT, drug therapy
- advanced cancer: RT, radiotherapy
- advanced cancer: SU, surgery
- genetic marker
- cancer combination chemotherapy
- quality of life
- diarrhea: SI, side effect
- mucosa inflammation: SI, side effect
- hand foot syndrome: SI, side effect
- bone marrow suppression: SI, side effect
- drug mechanism
- drug efficacy
- febrile neutropenia: SI, side effect
- stroke: SI, side effect
- heart infarction: SI, side effect
- cardiovascular disease: SI, side effect
- drug tolerability
- human
- clinical trial
- review
- Drug Descriptors:
- \*antineoplastic agent: AE, adverse drug reaction

\*antineoplastic agent: CT, clinical trial  
\*antineoplastic agent: CB, drug combination  
\*antineoplastic agent: CM, drug comparison  
\*antineoplastic agent: DT, drug therapy  
\*antineoplastic agent: PD, pharmacology  
\*antineoplastic agent: IV, intravenous drug administration  
\*antineoplastic agent: PO, oral drug administration  
irinotecan: AE, adverse drug reaction  
irinotecan: CT, clinical trial  
    **irinotecan: CB, drug combination**  
irinotecan: CM, drug comparison  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
oxaliplatin: AE, adverse drug reaction  
oxaliplatin: CT, clinical trial  
oxaliplatin: CB, drug combination  
oxaliplatin: CM, drug comparison  
oxaliplatin: DT, drug therapy  
oxaliplatin: PD, pharmacology  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: CB, drug combination  
fluorouracil: CM, drug comparison  
fluorouracil: DT, drug therapy  
fluorouracil: PD, pharmacology  
fluorouracil: IV, intravenous drug administration  
fluorouracil: PO, oral drug administration  
folinic acid: AE, adverse drug reaction  
folinic acid: CT, clinical trial  
folinic acid: CB, drug combination  
folinic acid: CM, drug comparison  
folinic acid: DT, drug therapy  
folinic acid: PD, pharmacology  
epidermal growth factor receptor: EC, endogenous compound  
vasculotropin inhibitor: AE, adverse drug reaction  
vasculotropin inhibitor: CT, clinical trial  
vasculotropin inhibitor: DT, drug therapy  
cyclooxygenase 2 inhibitor: AE, adverse drug reaction  
cyclooxygenase 2 inhibitor: CT, clinical trial  
cyclooxygenase 2 inhibitor: DT, drug therapy  
floxuridine phosphate  
levamisole: CT, clinical trial  
levamisole: CB, drug combination  
levamisole: DT, drug therapy  
edrecolomab: AE, adverse drug reaction  
edrecolomab: CT, clinical trial  
edrecolomab: CB, drug combination  
edrecolomab: CM, drug comparison  
edrecolomab: DT, drug therapy  
edrecolomab: PD, pharmacology  
capecitabine: AE, adverse drug reaction  
capecitabine: CT, clinical trial  
capecitabine: CB, drug combination  
capecitabine: CM, drug comparison  
capecitabine: DT, drug therapy  
capecitabine: PO, oral drug administration  
UFT: CT, clinical trial  
UFT: CB, drug combination  
UFT: CM, drug comparison  
UFT: DT, drug therapy  
fluoropyrimidine derivative: AE, adverse drug reaction  
fluoropyrimidine derivative: CT, clinical trial  
fluoropyrimidine derivative: CB, drug combination

fluoropyrimidine derivative: CM, drug comparison  
fluoropyrimidine derivative: DT, drug therapy  
fluoropyrimidine derivative: PO, oral drug administration  
gefitinib: CT, clinical trial  
gefitinib: CB, drug combination  
gefitinib: DT, drug therapy  
gefitinib: PD, pharmacology  
gefitinib: PO, oral drug administration  
erlotinib: CT, clinical trial  
erlotinib: DT, drug therapy  
erlotinib: PO, oral drug administration  
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6  
quinazolinyl]acrylamide: CT, clinical trial  
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6  
quinazolinyl]acrylamide: DT, drug therapy  
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6  
quinazolinyl]acrylamide: PO, oral drug administration  
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h  
pyrrolo[2,3 d]pyrimidine: CT, clinical trial  
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h  
pyrrolo[2,3 d]pyrimidine: DT, drug therapy  
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h  
pyrrolo[2,3 d]pyrimidine: PO, oral drug administration  
4 (3 chloro 4 fluoroanilino) 3 cyano 6 (4  
dimethylaminocrotonamido) 7 ethoxyquinoline: CT, clinical  
trial  
4 (3 chloro 4 fluoroanilino) 3 cyano 6 (4  
dimethylaminocrotonamido) 7 ethoxyquinoline: DT, drug  
therapy  
4 (3 chloro 4 fluoroanilino) 3 cyano 6 (4  
dimethylaminocrotonamido) 7 ethoxyquinoline: PO, oral drug  
administration  
protein tyrosine kinase inhibitor: CT, clinical trial  
protein tyrosine kinase inhibitor: DT, drug therapy  
protein tyrosine kinase inhibitor: PO, oral drug  
administration  
cetuximab: CT, clinical trial  
cetuximab: CB, drug combination  
cetuximab: DT, drug therapy  
cetuximab: PD, pharmacology  
cetuximab: IV, intravenous drug administration  
angiogenesis inhibitor: DT, drug therapy  
angiogenesis inhibitor: PD, pharmacology  
angiostatin: DT, drug therapy  
angiostatin: PD, pharmacology  
endostatin: DT, drug therapy  
endostatin: PD, pharmacology  
bevacizumab: CT, clinical trial  
bevacizumab: CB, drug combination  
bevacizumab: DT, drug therapy  
bevacizumab: PD, pharmacology  
bevacizumab: IV, intravenous drug administration  
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h  
indol 2 one: CT, clinical trial  
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h  
indol 2 one: DT, drug therapy  
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h  
indol 2 one: IV, intravenous drug administration  
celecoxib: AE, adverse drug reaction  
celecoxib: CT, clinical trial  
celecoxib: CB, drug combination  
celecoxib: CM, drug comparison  
celecoxib: DT, drug therapy

celecoxib: PD, pharmacology  
 rofecoxib: AE, adverse drug reaction  
 rofecoxib: CT, clinical trial  
 rofecoxib: DT, drug therapy  
 rofecoxib: PD, pharmacology  
 r 115777: CT, clinical trial  
 r 115777: DT, drug therapy  
 r 115777: PD, pharmacology  
 r 115777: PO, oral drug administration  
 unindexed drug  
 farnestra

CAS REGISTRY NO.: (irinotecan) 100286-90-6; (oxaliplatin) 61825-94-3;  
 (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2;  
 (floxuridine phosphate) 134-46-3; (levamisole) 14769-73-4,  
 16595-80-5; (capecitabine) 154361-50-9; (UFT) 74578-38-4;  
 (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7;  
 (erlotinib) 183319-69-9; (n [4 (3 chloro 4 fluoroanilino) 7  
 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide)  
 267243-28-7, 338796-35-3; (4 (3 chloro 4 fluoroanilino) 3  
 cyano 6 (4 dimethylaminocrotonamido) 7 ethoxyquinoline)  
 257933-82-7; (cetuximab) 205923-56-4; (angiostatin)  
 172642-30-7, 86090-08-6; (endostatin) 187888-07-9;  
 (bevacizumab) 216974-75-3; (3 [(3,5 dimethyl 1h pyrrol 2  
 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7;  
 (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7,  
 186912-82-3

CHEMICAL NAME: (1) Iressa; (2) Zd 1839; (3) Osi 774; (4) Tarceva; (5) C  
 225; (6) Erbitux; (7) Osi 774; (8) Tarceva; (9) Osi 774;  
 (10) Tarceva; (11) C 225; (12) Erbitux; (13) Avastin; (14)  
 R 115777; (15) Farnestra; (16) Vioxx; (17) Su 5416; Cpt 11;  
 Ci 1033; Pki 166; Ekb 569; Angiostatin; Endostatin;  
 Celebrex

COMPANY NAME: (2) Astra Zeneca; (4) Hoffmann La Roche; (6) Imclone; (10)  
 OSIP; (12) Bristol Myers Squibb; (13) Genentech; (15)  
 Johnson and Johnson; (16) Merck; (17) Sugen; Abgenix

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ACCESSION NUMBER: 2003339368 EMBASE

TITLE: Current review of chemotherapy for colorectal cancer: A  
 European perspective.

AUTHOR: Kohne C.-H.

CORPORATE SOURCE: Dr. C.-H. Kohne, Medizinische Klinik und Poliklinik I,  
 Univ. Klin. Carl Gustav Carus, Fetscherstr. 74, D-01307  
 Dresden, Germany

SOURCE: Biotherapy, (2003) 17/4 (368-378).  
 Refs: 54

ISSN: 0914-2223 CODEN: BITPE

COUNTRY: Japan

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

New drugs have improved efficacy or convenience of treatment in metastatic colorectal cancer. The oral fluoropyrimidines UFT and capecitabine mimic a protracted 5-FU administration and may avoid intravenous application. They are less toxic and equally effective as a modulated intravenous 5-FU bolus application. First-line therapy with irinotecan or oxaliplatin and 5-FU/folinic acid (FA) may induce an objective response in up to 50% of patients and allows

neoadjuvant concepts in unresectable liver metastasis. The combination therapy increased progression-free survival and irinotecan/5-FU/FA improved overall survival when compared to 5-FU/FA. Sequential treatment of infusional 5-FU plus oxaliplatin or irinotecan results in a median survival exceeding 20 months. A second-line therapy should be offered to all patients since both drugs are active, and irinotecan increased survival in phase III trials. New targets in treatment of colorectal cancer are the EGF and VEGF receptors. The monoclonal EGFR antibody cetuximab is active in second-line therapy and could induce a high response rate in first-line therapy, and is underdevelopment.

## CONTROLLED TERM:

## Medical Descriptors:

\*colorectal cancer: DT, drug therapy  
**cancer combination chemotherapy**  
 drug efficacy  
 liver metastasis: CO, complication  
 liver metastasis: DT, drug therapy  
 cancer survival  
 outcomes research  
 cancer adjuvant therapy  
 drug metabolism  
 drug safety  
 neutropenia: SI, side effect  
 stomatitis: SI, side effect  
 hand foot syndrome: SI, side effect  
 diarrhea: SI, side effect  
 abdominal cramp: SI, side effect  
 thromboembolism: SI, side effect  
 heart infarction: SI, side effect  
 lung embolism: SI, side effect  
 cerebrovascular disease: SI, side effect  
 drug mechanism  
 neurotoxicity: SI, side effect  
 thrombocytopenia: SI, side effect  
 cancer regression  
 oncogene neu  
 acne: SI, side effect  
 folliculitis: SI, side effect  
 human  
 clinical trial  
 review

## Drug Descriptors:

\*fluoropyrimidine derivative: AE, adverse drug reaction  
 \*fluoropyrimidine derivative: CT, clinical trial  
 \*fluoropyrimidine derivative: CB, drug combination  
 \*fluoropyrimidine derivative: CM, drug comparison  
 \*fluoropyrimidine derivative: DT, drug therapy  
 \*fluoropyrimidine derivative: PK, pharmacokinetics  
 \*UFT: AE, adverse drug reaction  
 \*UFT: CT, clinical trial  
 \*UFT: CB, drug combination  
 \*UFT: CM, drug comparison  
 \*UFT: DT, drug therapy  
 \*UFT: PK, pharmacokinetics  
 \*irinotecan: AE, adverse drug reaction  
 \*irinotecan: CT, clinical trial  
 \*irinotecan: CB, drug combination  
 \*irinotecan: CM, drug comparison  
 \*irinotecan: DT, drug therapy  
 \*irinotecan: PK, pharmacokinetics  
 \*irinotecan: PD, pharmacology  
 \*irinotecan: IV, intravenous drug administration  
 \*folinic acid: AE, adverse drug reaction  
 \*folinic acid: CT, clinical trial

\*folinic acid: CB, drug combination  
\*folinic acid: DT, drug therapy  
\*folinic acid: PK, pharmacokinetics  
\*folinic acid: IV, intravenous drug administration  
\*oxaliplatin: AE, adverse drug reaction  
\*oxaliplatin: CT, clinical trial  
\*oxaliplatin: CB, drug combination  
\*oxaliplatin: CM, drug comparison  
\*oxaliplatin: IT, drug interaction  
\*oxaliplatin: DT, drug therapy  
\*oxaliplatin: PK, pharmacokinetics  
\*oxaliplatin: PD, pharmacology  
\*oxaliplatin: IV, intravenous drug administration  
\*cetuximab: AE, adverse drug reaction  
\*cetuximab: CT, clinical trial  
\*cetuximab: CB, drug combination  
\*cetuximab: DT, drug therapy  
\*cetuximab: PK, pharmacokinetics  
\*cetuximab: PD, pharmacology  
epidermal growth factor  
vasculotropin  
monoclonal antibody  
capecitabine: AE, adverse drug reaction  
capecitabine: CT, clinical trial  
capecitabine: CB, drug combination  
capecitabine: DT, drug therapy  
capecitabine: PK, pharmacokinetics  
capecitabine: PD, pharmacology  
tegafur: AE, adverse drug reaction  
tegafur: CT, clinical trial  
tegafur: CB, drug combination  
tegafur: DT, drug therapy  
tegafur: PK, pharmacokinetics  
tegafur: PD, pharmacology  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: CB, drug combination  
fluorouracil: CM, drug comparison  
fluorouracil: IT, drug interaction  
fluorouracil: DT, drug therapy  
fluorouracil: PK, pharmacokinetics  
fluorouracil: PD, pharmacology  
fluorouracil: IV, intravenous drug administration  
loperamide  
antibiotic agent  
cyclooxygenase 2 inhibitor: CT, clinical trial  
cyclooxygenase 2 inhibitor: CB, drug combination  
cyclooxygenase 2 inhibitor: DT, drug therapy  
cyclooxygenase 2 inhibitor: PD, pharmacology  
epidermal growth factor receptor  
gefitinib: DT, drug therapy  
protein tyrosine kinase inhibitor: DT, drug therapy  
erlotinib: DT, drug therapy  
4 (3 chloro 4 fluoroanilino) 3 cyano 6 (4  
dimethylaminocrotonamido) 7 ethoxyquinoline: DT, drug  
therapy  
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h  
pyrrolo[2,3 d]pyrimidine: DT, drug therapy  
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6  
quinazolinyl]acrylamide: DT, drug therapy  
vasculotropin receptor  
bevacizumab: CT, clinical trial  
bevacizumab: CB, drug combination

bevacizumab: CM, drug comparison  
 bevacizumab: DT, drug therapy  
 1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DT,  
 drug therapy  
 3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h  
 indol 2 one: DT, drug therapy  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3  
 pyrrolepropionic acid: DT, drug therapy  
 (UFT) 74578-38-4; (irinotecan) 100286-90-6; (folinic acid)  
 58-05-9, 68538-85-2; (oxaliplatin) 61825-94-3; (cetuximab)  
 205923-56-4; (epidermal growth factor) 62229-50-9;  
 (vasculotropin) 127464-60-2; (capecitabine) 154361-50-9;  
 (tegafur) 17902-23-7; (fluorouracil) 51-21-8; (loperamide)  
 34552-83-5, 53179-11-6; (gefitinib) 184475-35-2,  
 184475-55-6, 184475-56-7; (erlotinib) 183319-69-9; (4 (3  
 chloro 4 fluoroanilino) 3 cyano 6 (4  
 dimethylaminocrotonamido) 7 ethoxyquinoline) 257933-82-7;  
 (n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6  
 quinazolinyl]acrylamide) 267243-28-7, 338796-35-3;  
 (vasculotropin receptor) 301253-48-5; (bevacizumab)  
 216974-75-3; (1 (4 chloroanilino) 4 (4  
 pyridylmethyl)phthalazine) 212142-18-2; (3 [(3,5 dimethyl  
 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one)  
 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene)  
 3 pyrrolepropionic acid) 252916-29-3  
 CAS REGISTRY NO.:  
 CHEMICAL NAME: Osi 774; Ekb 569; Pki 166; Ci 1033; Zd 1839; Ptk 787; Su  
 5416; Su 6668

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ACCESSION NUMBER: 2003267460 EMBASE  
 TITLE: Role of cyclooxygenase-2 inhibitors in combination with  
 radiation therapy in lung cancer.  
 AUTHOR: Liao Z.; Komaki R.; Mason K.A.; Milas L.  
 CORPORATE SOURCE: Dr. Z. Liao, Division of Radiation Oncology, University of  
 Texas, M. D. Anderson Cancer Center, 1515 Holcombe Blvd,  
 Houston, TX 77030, United States. zliao@mdanderson.org  
 SOURCE: Clinical Lung Cancer, (2003) 4/6 (356-365).  
 Refs: 114  
 ISSN: 1525-7304 CODEN: CLCLCA  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 014 Radiology  
 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ABSTRACT:

Cyclooxygenase-2 (COX-2) is an enzyme involved in prostaglandin production in  
 pathologic states such as inflammatory disorders and cancer. The enzyme is  
 often overexpressed in premalignant lesions and cancer of the lung.  
 Overexpression of COX-2 in lung cancer is associated with more aggressive  
 biological tumor behavior and adverse patient outcome. In preclinical studies,  
 inhibition of this enzyme with selective COX-2 inhibitors enhances tumor  
 response to radiation and chemotherapeutic agents. These findings have been  
 rapidly advanced to clinical oncology. Clinical trials of the combination of  
 selective COX-2 inhibitors with radiation therapy, chemotherapy, or both in  
 patients with lung cancer have been initiated and some preliminary results are  
 available. In this review, we describe the relationship between overexpression  
 of COX-2 and lung cancer, the antitumor effect of selective COX-2 inhibitors,

discuss the rationale for using selective COX-2 inhibitors combined with radiation therapy and chemotherapy, and summarize current clinical protocols and initial findings.

CONTROLLED TERM: Medical Descriptors:

- \*lung cancer: DT, drug therapy
- \*lung cancer: RT, radiotherapy
- prostaglandin synthesis
- gene overexpression
- precancer**
- treatment outcome
- enzyme inhibition
- clinical protocol
- radiosensitivity
- drug effect
- drug efficacy
- drug mechanism
- drug potentiation**
- dose response
- maximum tolerated dose
- antineoplastic activity**
- gastrointestinal toxicity: SI, side effect
- diarrhea: SI, side effect
- digestive system ulcer: SI, side effect
- gastrointestinal hemorrhage: SI, side effect
- heart infarction: SI, side effect
- esophagitis: CO, complication
- esophagitis: SI, side effect
- pneumonia: CO, complication
- pneumonia: SI, side effect
- human
- nonhuman
- clinical trial
- review

Drug Descriptors:

- \*cyclooxygenase 2 inhibitor: AE, adverse drug reaction
- \*cyclooxygenase 2 inhibitor: CT, clinical trial
- \*cyclooxygenase 2 inhibitor: CB, drug combination**
- \*cyclooxygenase 2 inhibitor: CM, drug comparison
- \*cyclooxygenase 2 inhibitor: DO, drug dose
- \*cyclooxygenase 2 inhibitor: IT, drug interaction
- \*cyclooxygenase 2 inhibitor: DT, drug therapy
- \*cyclooxygenase 2 inhibitor: PD, pharmacology
- cyclooxygenase 2: EC, endogenous compound
- prostaglandin: EC, endogenous compound
- nonsteroid antiinflammatory agent: AE, adverse drug reaction
- nonsteroid antiinflammatory agent: CM, drug comparison
- nonsteroid antiinflammatory agent: DT, drug therapy
- nonsteroid antiinflammatory agent: PD, pharmacology
- n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide: DT, drug therapy
- n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide: PD, pharmacology
- celecoxib: AE, adverse drug reaction
- celecoxib: CT, clinical trial
- celecoxib: CM, drug comparison
- celecoxib: DO, drug dose
- celecoxib: DT, drug therapy
- celecoxib: PD, pharmacology
- indometacin: AE, adverse drug reaction
- indometacin: DT, drug therapy
- indometacin: PD, pharmacology

prostaglandin inhibitor: AE, adverse drug reaction  
prostaglandin inhibitor: CT, clinical trial  
prostaglandin inhibitor: CB, drug combination  
prostaglandin inhibitor: CM, drug comparison  
prostaglandin inhibitor: DO, drug dose  
prostaglandin inhibitor: IT, drug interaction  
prostaglandin inhibitor: DT, drug therapy  
prostaglandin inhibitor: PD, pharmacology  
ibuprofen: AE, adverse drug reaction  
ibuprofen: CM, drug comparison  
ibuprofen: DT, drug therapy  
ibuprofen: PD, pharmacology  
4 [5 (4 chlorophenyl) 3 trifluoromethyl 1h pyrazol 1  
yl]benzenesulfonamide: DT, drug therapy  
4 [5 (4 chlorophenyl) 3 trifluoromethyl 1h pyrazol 1  
yl]benzenesulfonamide: PD, pharmacology  
angiogenesis inhibitor: AE, adverse drug reaction  
angiogenesis inhibitor: CT, clinical trial  
angiogenesis inhibitor: CB, drug combination  
angiogenesis inhibitor: CM, drug comparison  
angiogenesis inhibitor: DO, drug dose  
angiogenesis inhibitor: IT, drug interaction  
angiogenesis inhibitor: DT, drug therapy  
angiogenesis inhibitor: PD, pharmacology  
anthracycline derivative: CB, drug combination  
anthracycline derivative: IT, drug interaction  
anthracycline derivative: DT, drug therapy  
anthracycline derivative: PD, pharmacology  
doxorubicin: CB, drug combination  
doxorubicin: IT, drug interaction  
doxorubicin: DT, drug therapy  
doxorubicin: PD, pharmacology  
daunorubicin: CB, drug combination  
daunorubicin: IT, drug interaction  
daunorubicin: DT, drug therapy  
daunorubicin: PD, pharmacology  
epirubicin: CB, drug combination  
epirubicin: IT, drug interaction  
epirubicin: DT, drug therapy  
epirubicin: PD, pharmacology  
irinotecan: AE, adverse drug reaction  
**irinotecan: CB, drug combination**  
irinotecan: IT, drug interaction  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
diclofenac: AE, adverse drug reaction  
diclofenac: CM, drug comparison  
diclofenac: DT, drug therapy  
diclofenac: PD, pharmacology  
rofecoxib: AE, adverse drug reaction  
rofecoxib: CM, drug comparison  
rofecoxib: DT, drug therapy  
rofecoxib: PD, pharmacology  
naproxen: AE, adverse drug reaction  
naproxen: CM, drug comparison  
naproxen: DT, drug therapy  
naproxen: PD, pharmacology  
docetaxel: CT, clinical trial  
docetaxel: CB, drug combination  
docetaxel: DT, drug therapy  
docetaxel: PD, pharmacology  
carboplatin: AE, adverse drug reaction  
carboplatin: CT, clinical trial

carboplatin: CB, drug combination  
 carboplatin: DT, drug therapy  
 carboplatin: PD, pharmacology  
 paclitaxel: AE, adverse drug reaction  
 paclitaxel: CT, clinical trial  
 paclitaxel: CB, drug combination  
 paclitaxel: DT, drug therapy  
 paclitaxel: PD, pharmacology

CAS REGISTRY NO.: (n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide)  
 123653-11-2; (celecoxib) 169590-42-5; (indometacin)  
 53-86-1, 74252-25-8, 7681-54-1; (ibuprofen) 15687-27-1; (4  
 [5 (4 chlorophenyl) 3 trifluoromethyl 1h pyrazol 1  
 yl]benzenesulfonamide) 170569-86-5; (doxorubicin)  
 23214-92-8, 25316-40-9; (daunorubicin) 12707-28-7,  
 20830-81-3, 23541-50-6; (epirubicin) 56390-09-1,  
 56420-45-2; (irinotecan) 100286-90-6; (diclofenac)  
 15307-79-6, 15307-86-5; (rofecoxib) 162011-90-7,  
 186912-82-3; (naproxen) 22204-53-1, 26159-34-2; (docetaxel)  
 114977-28-5; (carboplatin) 41575-94-4; (paclitaxel)  
 33069-62-4

CHEMICAL NAME: Ns 398; Sc 236

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ACCESSION NUMBER: 2003359485 EMBASE  
 TITLE: Targeted therapies: Focus on a new strategy for  
 gastrointestinal tumors.  
 AUTHOR: Nicoletta D.; Maione P.; Gridelli C.  
 CORPORATE SOURCE: C. Gridelli, Division of Medical Oncology, 'S.G. Moscati'  
 Hospital, Via Circumvallazione, Avellino 83100, Italy.  
 cgridelli@libero.it  
 SOURCE: Critical Reviews in Oncology/Hematology, (1 Sep 2003) 47/3  
 (261-271).  
 Refs: 70  
 ISSN: 1040-8428 CODEN: CCRHEC  
 COUNTRY: Ireland  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 048 Gastroenterology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ABSTRACT:

In the last few years the knowledge of molecular oncology has led to the development of many new biological agents whose targets are extracellular or intracellular molecules involved in the main signalling pathways that play major roles in cancer development. These agents represent a new approach to gastrointestinal malignancies, as for many other types of tumors; preliminary data show that targeted therapy may enhance activity of chemotherapeutic agents (i.e. cetuximab in metastatic colorectal cancer (CRC)) or be active as monotherapy (i.e. imatinib in gastro-intestinal stromal tumors). Despite the encouraging preclinical results, the majority of these compounds have not yet produced convincing clinical results. However, these new agents raise a new challenge in the treatment of gastrointestinal cancers, especially for CRC.  
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CONTROLLED TERM: Medical Descriptors:  
 \*gastrointestinal tumor: DT, drug therapy  
 \*colorectal carcinoma: DT, drug therapy  
 \*cancer chemotherapy  
 signal transduction

cancer patient  
acne: SI, side effect  
allergic reaction: SI, side effect  
rash: SI, side effect  
folliculitis: SI, side effect  
diarrhea: SI, side effect  
neutropenia: SI, side effect  
breast carcinoma: DT, drug therapy  
gastrointestinal symptom: SI, side effect  
abdominal pain: SI, side effect  
nausea: SI, side effect  
skin toxicity: SI, side effect  
gastrointestinal toxicity: SI, side effect  
blood toxicity: SI, side effect  
chemotherapy induced emesis: SI, side effect  
edema: SI, side effect  
ankle edema: SI, side effect  
peripheral edema: SI, side effect  
drug tolerability  
fatigue: SI, side effect  
bone marrow suppression: SI, side effect  
malaise: SI, side effect  
anemia: SI, side effect  
deep vein thrombosis: SI, side effect  
liver metastasis: DT, drug therapy  
constipation: SI, side effect  
peripheral neuropathy: SI, side effect  
polyarthrititis: SI, side effect  
human  
clinical trial  
review  
Drug Descriptors:  
\*epidermal growth factor receptor antibody: AE, adverse  
drug reaction  
\*epidermal growth factor receptor antibody: CT, clinical  
trial  
\*epidermal growth factor receptor antibody: CB, drug  
combination  
\*epidermal growth factor receptor antibody: DT, drug  
therapy  
\*protein farnesyltransferase inhibitor: AE, adverse drug  
reaction  
\*protein farnesyltransferase inhibitor: CT, clinical trial  
\*protein farnesyltransferase inhibitor: DT, drug therapy  
\*protein farnesyltransferase inhibitor: PD, pharmacology  
\*angiogenesis inhibitor: AE, adverse drug reaction  
\*angiogenesis inhibitor: CT, clinical trial  
\*angiogenesis inhibitor: CB, drug combination  
\*angiogenesis inhibitor: DT, drug therapy  
\*angiogenesis inhibitor: PD, pharmacology  
\*cyclooxygenase 2 inhibitor: CT, clinical trial  
\***cyclooxygenase 2 inhibitor: CB, drug combination**  
\*cyclooxygenase 2 inhibitor: DT, drug therapy  
\*matrix metalloproteinase inhibitor: AE, adverse drug  
reaction  
\*matrix metalloproteinase inhibitor: CT, clinical trial  
\*matrix metalloproteinase inhibitor: CB, drug combination  
\*matrix metalloproteinase inhibitor: DO, drug dose  
\*matrix metalloproteinase inhibitor: DT, drug therapy  
cetuximab: AE, adverse drug reaction  
cetuximab: CT, clinical trial  
cetuximab: CB, drug combination  
cetuximab: DT, drug therapy

trastuzumab: CT, clinical trial  
trastuzumab: CB, drug combination  
trastuzumab: DT, drug therapy  
edrecolomab: AE, adverse drug reaction  
edrecolomab: CT, clinical trial  
edrecolomab: CB, drug combination  
edrecolomab: DT, drug therapy  
edrecolomab: IV, intravenous drug administration  
gefitinib: AE, adverse drug reaction  
gefitinib: CT, clinical trial  
gefitinib: CB, drug combination  
gefitinib: DO, drug dose  
gefitinib: DT, drug therapy  
gefitinib: PO, oral drug administration  
imatinib: AE, adverse drug reaction  
imatinib: CT, clinical trial  
imatinib: DT, drug therapy  
imatinib: PO, oral drug administration  
bevacizumab: AE, adverse drug reaction  
bevacizumab: CT, clinical trial  
bevacizumab: CB, drug combination  
bevacizumab: DT, drug therapy  
bevacizumab: PD, pharmacology  
bevacizumab: IV, intravenous drug administration  
thalidomide: AE, adverse drug reaction  
thalidomide: CT, clinical trial  
thalidomide: CB, drug combination  
thalidomide: DO, drug dose  
thalidomide: DT, drug therapy  
thalidomide: IV, intravenous drug administration  
**irinotecan: CB, drug combination**  
irinotecan: DT, drug therapy  
irinotecan: IV, intravenous drug administration  
fluorouracil: CB, drug combination  
fluorouracil: DT, drug therapy  
isis 2503: PD, pharmacology  
r 115777: AE, adverse drug reaction  
r 115777: CT, clinical trial  
r 115777: CB, drug combination  
r 115777: DT, drug therapy  
r 115777: PD, pharmacology  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: AE, adverse drug  
reaction  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: CT, clinical trial  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: CB, drug combination  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: DT, drug therapy  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: PD, pharmacology  
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h  
benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2  
oxoethyl] 1 piperidinecarboxamide: PO, oral drug  
administration  
cgp 69846a: PD, pharmacology  
gemcitabine: CB, drug combination

gemcitabine: DT, drug therapy  
vasculotropin antibody: CT, clinical trial  
vasculotropin antibody: DO, drug dose  
vasculotropin antibody: DT, drug therapy  
vasculotropin antibody: PD, pharmacology  
marimastat: AE, adverse drug reaction  
marimastat: CT, clinical trial  
marimastat: CB, drug combination  
marimastat: DO, drug dose  
marimastat: DT, drug therapy  
    **celecoxib: CB, drug combination**  
celecoxib: DT, drug therapy  
erlotinib  
zarnestra  
lonafarnib  
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4  
ylmethyl) 4 (2 thienylsulfonfyl) 1h 1,4 benzodiazepine  
ci 1040  
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3  
pyrrolepropionic acid  
zd 6474

CAS REGISTRY NO.: (cetuximab) 205923-56-4; (trastuzumab) 180288-69-1;  
(gefitinib) 184475-35-2, 184475-55-6, 184475-56-7;  
(imatinib) 152459-95-5, 220127-57-1; (bevacizumab)  
216974-75-3; (thalidomide) 50-35-1; (irinotecan)  
100286-90-6; (fluorouracil) 51-21-8; (isis 2503)  
149957-14-2; (4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro  
5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl]  
2 oxoethyl] 1 piperidinecarboxamide) 193275-84-2; (cgp  
69846a) 177075-18-2; (gemcitabine) 103882-84-4;  
(marimastat) 154039-60-8; (celecoxib) 169590-42-5;  
(erlotinib) 183319-69-9; (3 benzyl 7 cyano 2,3,4,5  
tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonfyl)  
1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (2,4  
dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3  
pyrrolepropionic acid) 252916-29-3  
CHEMICAL NAME: Marimastat; Zd 6474; Su 6668; Avastin; Ci 1040; Isis 5132;  
Bms 214662; Lonafarnib; Zarnestra; Isis 2503; Tarceva;  
Panorex; Herceptin; Erbitux; Gleevec; Iressa

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ACCESSION NUMBER: 2003051342 EMBASE  
TITLE: Cyclooxygenase 2: A molecular target for cancer prevention  
and treatment.  
AUTHOR: Subbaramaiah K.; Dannenberg A.J.  
CORPORATE SOURCE: A.J. Dannenberg, Weill Med. Coll. of Cornell Univ., Dept.  
of Medicine, 525 East 68th Street, New York, NY 10021,  
United States. ajdannenberg@med.cornell.edu  
SOURCE: Trends in Pharmacological Sciences, (1 Feb 2003) 24/2  
(96-102).  
Refs: 66  
ISSN: 0165-6147 CODEN: TPHSDY  
PUBLISHER IDENT.: S 0165-6147(02)00043-3  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT:

Cyclooxygenase2 (COX-2), an inducible prostaglandin G/H synthase, is overexpressed in several human cancers. Here, the potential utility of selective COX-2 inhibitors in the prevention and treatment of cancer is considered. The mechanisms by which COX-2 levels increase in cancers, key data that indicate a causal link between increased COX-2 activity and tumorigenesis, and possible mechanisms of action of COX-2 are discussed. In a proof-of-principle clinical trial, treatment with the selective COX-2 inhibitor celecoxib reduced the number of colorectal polyps in patients with familial adenomatous polyposis. Selective COX-2 inhibitors appear to be sufficiently safe to permit large-scale clinical testing and numerous clinical trials are currently under way to determine whether selective inhibitors of COX-2 are effective in the prevention and treatment of cancer.

CONTROLLED TERM: Medical Descriptors:

- \*cancer chemotherapy**
- \*cancer prevention
- \*colorectal carcinoma: DT, drug therapy
- \*lung non small cell cancer: DT, drug therapy
- \*prostate carcinoma: DT, drug therapy
- drug targeting
- enzyme activity
- carcinogenesis
- adenomatous polyp: DT, drug therapy
- prostaglandin synthesis
- protein expression
- multidrug resistance
- transcription regulation
- human
- clinical trial
- review
- priority journal
- Drug Descriptors:
- \*cyclooxygenase 2: EC, endogenous compound
- cyclooxygenase 2 inhibitor: CT, clinical trial
- cyclooxygenase 2 inhibitor: CB, drug combination**
- cyclooxygenase 2 inhibitor: DT, drug therapy
- cyclooxygenase 2 inhibitor: PD, pharmacology
- celecoxib: CT, clinical trial
- celecoxib: CB, drug combination**
- celecoxib: DT, drug therapy
- celecoxib: PD, pharmacology
- irinotecan: CT, clinical trial
- irinotecan: CB, drug combination**
- irinotecan: DT, drug therapy
- irinotecan: PD, pharmacology
- fluorouracil: CT, clinical trial
- fluorouracil: CB, drug combination
- fluorouracil: DT, drug therapy
- fluorouracil: PD, pharmacology
- folinic acid: CT, clinical trial
- folinic acid: CB, drug combination
- folinic acid: DT, drug therapy
- folinic acid: PD, pharmacology
- paclitaxel: CT, clinical trial
- paclitaxel: CB, drug combination
- paclitaxel: DT, drug therapy
- paclitaxel: PD, pharmacology
- carboplatin: CT, clinical trial
- carboplatin: CB, drug combination
- carboplatin: DT, drug therapy
- carboplatin: PD, pharmacology

CAS REGISTRY NO.: (celecoxib) 169590-42-5; (irinotecan) 100286-90-6;  
(fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2;

(paclitaxel) 33069-62-4; (carboplatin) 41575-94-4

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ACCESSION NUMBER: 2003344739 EMBASE  
TITLE: [Controversies of colon cancer adjuvant treatment].  
CANCRO DO COLON: CONTROVERSIAS DO TRATAMENTO ADJUVANTE.  
AUTHOR: Angelico V.M.; Costa N.M.; Fragoso M.; Sanches E.  
CORPORATE SOURCE: Dr. V.M. Angelico, Departamento de Oncologia Medica,  
Instituto Portugues de Oncologia, Centro do Porto, R. Dr.  
Antonio Bernardino de Almeida, 4200 - 072 Porto, Portugal.  
nunomatoscosta@netcabo.pt  
SOURCE: Arquivos de Medicina, (2003) 17/1-3 (47-54).  
Refs: 55  
ISSN: 0871-3413 CODEN: ARQME3  
COUNTRY: Portugal  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 006 Internal Medicine  
016 Cancer  
037 Drug Literature Index  
048 Gastroenterology  
LANGUAGE: Portuguese  
SUMMARY LANGUAGE: English; Portuguese  
ABSTRACT:

The authors describe the evolution of adjuvant treatment of colon cancer in the last years. Based on the main published studies, we present a short historical revision about the use of chemotherapy in the adjuvant setting of colon cancer, Stages II and III (AJCC), referring the established consensus as well as the controversies. We enhance the main controversies that lead to the current treatment options. The clinical and biological factors with prognostic predictive value in terms of disease-free and overall survival are described, as well as some molecular and genetic markers which will might be used in order to identify groups of patients with a higher risk of tumoral recurrence. We still describe shortly the future directions in the adjuvant setting, namely, new cytotoxic agents (oral fluoropyrimidines, irinotecan or CPT-11, oxaliplatin), and biochemical or molecular target-based therapy (cyclo-oxygenase 2 inhibitors, monoclonal antibodies directed to determined tumoral antigens, such as edrecolomab and CeaVac).

CONTROLLED TERM: Medical Descriptors:  
\*colon cancer: DT, drug therapy  
\***cancer combination chemotherapy**  
\*cancer adjuvant therapy  
cancer staging  
prognosis  
cancer survival  
molecular interaction  
genetic marker  
tumor recurrence  
high risk population  
drug effect  
molecular genetics  
enzyme inhibition  
human  
review  
Drug Descriptors:  
\*cytotoxic agent: CB, drug combination  
\*cytotoxic agent: DT, drug therapy  
\*fluoropyrimidine: AN, drug analysis  
\*fluoropyrimidine: DT, drug therapy  
\*fluoropyrimidine: PO, oral drug administration  
\***irinotecan: CB, drug combination**  
\*irinotecan: DT, drug therapy

\*oxaliplatin: CB, drug combination  
\*oxaliplatin: DT, drug therapy  
cyclooxygenase 2 inhibitor: CB, drug combination  
cyclooxygenase 2 inhibitor: DT, drug therapy  
monoclonal antibody  
tumor antigen  
edrecolomab: CB, drug combination  
edrecolomab: DT, drug therapy  
CAS REGISTRY NO.: (fluoropyrimidine) 675-21-8; (irinotecan) 100286-90-6;  
(oxaliplatin) 61825-94-3  
CHEMICAL NAME: Cpt 11

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ACCESSION NUMBER: 2003294016 EMBASE  
TITLE: Irinotecan in metastatic colorectal cancer: Dose intensification and combination with new agents, including biological response modifiers.  
AUTHOR: Ducreux M.; Kohne C.-H.; Schwartz G.K.; Vanhoefer U.  
CORPORATE SOURCE: Dr. C.-H. Kohne, University Clinic of Carl-Gustav, Technical University of Dresden, Fetscherstrasse 74, 01307 Dresden, France. koehne@mkl.med.tu-dresden.de  
SOURCE: Annals of Oncology, (2003) 14/SUPPL. 2 (ii17-ii23).  
Refs: 41  
ISSN: 0923-7534 CODEN: ANONE2  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Phase I/II studies suggest that the combination of irinotecan with capecitabine is feasible and has promising activity. Diarrhea and neutropenia are dose limiting. Overall response rates (RRs) in the 40% to 60% range are seen from preliminary data. Work in progress is assessing the combination of irinotecan with UFT/leucovorin (LV). The use of irinotecan together with raltitrexed is also being investigated, as is its combination with oxaliplatin. Two phase II studies of irinotecan plus oxaliplatin in second-line patients report median survivals of 11-12 months. It seems possible to safely escalate the dose of single-agent irinotecan to 500 mg/m<sup>2</sup> in patients showing good tolerance of the drug. Irinotecan can be used in combination with LV5FU2 at doses up to 260 mg/m<sup>2</sup>, especially if only one bolus of 5-fluorouracil (5-FU) is given. Control of tumor growth is achieved in 90% of patients. Preliminary data suggest that regimens based on 5-FU/LV and irinotecan can safely be combined with the anti-epidermal growth factor receptor (EGFR) antibody cetuximab. In patients with EGFR-positive tumors, this may prove an effective means of increasing response rate or combating treatment resistance. Following evidence that COX-2 inhibition can slow progression in familial adenomatous polyposis, celecoxib is to be studied in metastatic colorectal cancer (CRC). In vitro, the cyclin-dependent kinase inhibitor flavopiridol enhances the induction of apoptosis by chemotherapy. Clinically, it can safely be administered with irinotecan, and studies in CRC are planned.

CONTROLLED TERM: Medical Descriptors:  
\*colorectal cancer: DT, drug therapy  
cancer combination chemotherapy  
drug megadose  
metastasis: DT, drug therapy  
drug dose regimen

drug activity  
dose response  
diarrhea: SI, side effect  
neutropenia: SI, side effect  
cancer survival  
drug safety  
drug tolerance  
cancer inhibition  
enzyme inhibition  
cancer growth  
adenomatous polyp: DT, drug therapy  
in vitro study  
apoptosis  
asthenia: SI, side effect  
febrile neutropenia: SI, side effect  
nausea: SI, side effect  
gastrointestinal toxicity: SI, side effect  
human  
clinical trial  
article  
priority journal  
Drug Descriptors:  
\*irinotecan: AE, adverse drug reaction  
\*irinotecan: CT, clinical trial  
    \*irinotecan: CB, drug combination  
\*irinotecan: CM, drug comparison  
\*irinotecan: DO, drug dose  
\*irinotecan: DT, drug therapy  
\*irinotecan: PD, pharmacology  
\*irinotecan: PO, oral drug administration  
capecitabine: AE, adverse drug reaction  
capecitabine: CT, clinical trial  
capecitabine: CB, drug combination  
capecitabine: DO, drug dose  
capecitabine: DT, drug therapy  
capecitabine: PD, pharmacology  
UFT: CT, clinical trial  
UFT: CB, drug combination  
UFT: DT, drug therapy  
UFT: PD, pharmacology  
folinic acid: CT, clinical trial  
folinic acid: CB, drug combination  
folinic acid: DT, drug therapy  
folinic acid: PD, pharmacology  
raltitrexed: AE, adverse drug reaction  
raltitrexed: CT, clinical trial  
raltitrexed: CB, drug combination  
raltitrexed: DO, drug dose  
raltitrexed: DT, drug therapy  
raltitrexed: PD, pharmacology  
oxaliplatin: CT, clinical trial  
oxaliplatin: CB, drug combination  
oxaliplatin: DO, drug dose  
oxaliplatin: DT, drug therapy  
oxaliplatin: PD, pharmacology  
fluorouracil: DO, drug dose  
fluorouracil: DT, drug therapy  
fluorouracil: PD, pharmacology  
cetuximab: CB, drug combination  
cetuximab: DO, drug dose  
cetuximab: DT, drug therapy  
cetuximab: PD, pharmacology  
cyclooxygenase 2: EC, endogenous compound

celecoxib: DT, drug therapy  
 cyclin dependent kinase inhibitor: PD, pharmacology  
 flavopiridol: CB, drug combination  
 flavopiridol: CM, drug comparison  
 flavopiridol: DO, drug dose  
 flavopiridol: DT, drug therapy  
 flavopiridol: PD, pharmacology  
 loperamide: CB, drug combination  
 loperamide: DO, drug dose  
 loperamide: DT, drug therapy

**cyclooxygenase 2 inhibitor: CB, drug combination**  
 cyclooxygenase 2 inhibitor: DT, drug therapy  
 cyclooxygenase 2 inhibitor: PD, pharmacology  
 docetaxel: CB, drug combination  
 docetaxel: DT, drug therapy  
 erlotinib: PD, pharmacology  
 gefitinib: PD, pharmacology

CAS REGISTRY NO.: (irinotecan) 100286-90-6; (capecitabine) 154361-50-9; (UFT) 74578-38-4; (folinic acid) 58-05-9, 68538-85-2; (raltitrexed) 112887-68-0; (oxaliplatin) 61825-94-3; (fluorouracil) 51-21-8; (cetuximab) 205923-56-4; (celecoxib) 169590-42-5; (flavopiridol) 146426-40-6; (loperamide) 34552-83-5, 53179-11-6; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7 )

CHEMICAL NAME: Imc c225; Osi 774; Iressa

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ACCESSION NUMBER: 2003375385 EMBASE

TITLE: Current and ongoing trials with irinotecan in the United States.

AUTHOR: Fuchs C.S.

CORPORATE SOURCE: Dr. C.S. Fuchs, Dana Farber Cancer Institute, 44 Binney St, Boston, MA 02115, United States

SOURCE: Seminars in Oncology, (2003) 30/4 SUPPL. 12 (9-17).

Refs: 28

ISSN: 0093-7754 CODEN: SOLGAV

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 048 Gastroenterology

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
 \*colorectal cancer: DT, drug therapy  
 \*advanced cancer: DT, drug therapy  
 metastasis: DT, drug therapy  
 cancer survival  
 drug infusion  
 disease course  
 granulocytopenia: SI, side effect  
 diarrhea: SI, side effect  
 bolus injection  
 drug mechanism  
 drug tolerability  
 neutropenia: SI, side effect  
 drug efficacy  
 drug potentiation  
 treatment failure

gastrointestinal symptom: SI, side effect  
neurotoxicity: SI, side effect  
cancer adjuvant therapy  
human

clinical trial  
conference paper  
priority journal

## Drug Descriptors:

\*irinotecan: AE, adverse drug reaction  
\*irinotecan: CT, clinical trial  
\*irinotecan: CB, drug combination  
\*irinotecan: IT, drug interaction  
\*irinotecan: DT, drug therapy  
\*irinotecan: PD, pharmacology  
\*irinotecan: IV, intravenous drug administration  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: CB, drug combination  
fluorouracil: DT, drug therapy  
fluorouracil: IV, intravenous drug administration  
folinic acid: AE, adverse drug reaction  
folinic acid: CT, clinical trial  
folinic acid: CB, drug combination  
folinic acid: DT, drug therapy  
folinic acid: IV, intravenous drug administration  
capecitabine: AE, adverse drug reaction  
capecitabine: CT, clinical trial  
capecitabine: CB, drug combination  
capecitabine: IT, drug interaction  
capecitabine: DT, drug therapy  
capecitabine: PD, pharmacology  
capecitabine: PO, oral drug administration  
celecoxib: AE, adverse drug reaction  
celecoxib: CT, clinical trial  
celecoxib: CB, drug combination  
celecoxib: IT, drug interaction  
celecoxib: DT, drug therapy  
celecoxib: PD, pharmacology  
oxaliplatin: AE, adverse drug reaction  
oxaliplatin: CB, drug combination  
oxaliplatin: DT, drug therapy  
cetuximab: CT, clinical trial  
cetuximab: CB, drug combination  
cetuximab: DT, drug therapy

CAS REGISTRY NO.: (irinotecan) 100286-90-6; (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2; (capecitabine) 154361-50-9; (celecoxib) 169590-42-5; (oxaliplatin) 61825-94-3; (cetuximab) 205923-56-4  
CHEMICAL NAME: (1) Erbitux; (2) C 225  
COMPANY NAME: (2) Imclone (United States); Pharmacia (United States)

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ACCESSION NUMBER: 2003375384 EMBASE  
TITLE: COX-2 inhibitors in oncology.  
AUTHOR: Haller D.G.  
CORPORATE SOURCE: Dr. D.G. Haller, Univ. of Pennsylvania Cancer Center, 16 Penn Tower, 3400 Spruce St, Philadelphia, PA 19104, United States  
SOURCE: Seminars in Oncology, (2003) 30/4 SUPPL. 12 (2-8).  
Refs: 36  
ISSN: 0093-7754 CODEN: SOLGAV  
COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 016 Cancer  
026 Immunology, Serology and Transplantation  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
CONTROLLED TERM: Medical Descriptors:  
\*cancer: DT, drug therapy  
\*cancer: ET, etiology  
\*cancer: PC, prevention  
carcinogenesis  
cancer prevention  
drug indication  
prognosis  
    **antineoplastic activity**  
colorectal cancer: ET, etiology  
stomach cancer: ET, etiology  
pancreas cancer: ET, etiology  
esophagus cancer: ET, etiology  
drug safety  
drug tolerability  
neutropenia: SI, side effect  
diarrhea: SI, side effect  
dose response  
    **cancer combination chemotherapy**  
neuropathy: SI, side effect  
hand foot syndrome: SI, side effect  
pain: SI, side effect  
drug mechanism  
human  
clinical trial  
conference paper  
priority journal  
Drug Descriptors:  
\*cyclooxygenase 2 inhibitor: CT, clinical trial  
\*cyclooxygenase 2 inhibitor: DT, drug therapy  
\*cyclooxygenase 2 inhibitor: PD, pharmacology  
cyclooxygenase 2  
cyclooxygenase 1  
celecoxib: CT, clinical trial  
    **celecoxib: CB, drug combination**  
celecoxib: DO, drug dose  
celecoxib: IT, drug interaction  
celecoxib: DT, drug therapy  
celecoxib: PD, pharmacology  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: CB, drug combination  
fluorouracil: CM, drug comparison  
fluorouracil: IT, drug interaction  
fluorouracil: DT, drug therapy  
fluorouracil: PO, oral drug administration  
irinotecan: AE, adverse drug reaction  
irinotecan: CT, clinical trial  
    **irinotecan: CB, drug combination**  
irinotecan: CM, drug comparison  
irinotecan: DO, drug dose  
irinotecan: IT, drug interaction  
irinotecan: DT, drug therapy  
folinic acid: AE, adverse drug reaction  
folinic acid: CB, drug combination

folinic acid: IT, drug interaction  
folinic acid: DT, drug therapy  
glutamine: AE, adverse drug reaction  
glutamine: CB, drug combination  
glutamine: IT, drug interaction  
glutamine: DT, drug therapy  
capecitabine: AE, adverse drug reaction  
capecitabine: IT, drug interaction  
capecitabine: DT, drug therapy  
CAS REGISTRY NO.: (celecoxib) 169590-42-5; (fluorouracil) 51-21-8;  
(irinotecan) 100286-90-6; (folinic acid) 58-05-9,  
68538-85-2; (glutamine) 56-85-9, 6899-04-3; (capecitabine)  
154361-50-9

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ACCESSION NUMBER: 2002297258 EMBASE  
TITLE: Chemosensitization of solid tumor cells by alteration of  
their susceptibility to apoptosis.  
AUTHOR: Cree I.A.; Knight L.; Di Nicolantonio F.; Sharma S.;  
Gulliford T.  
CORPORATE SOURCE: I.A. Cree, Department of Histopathology, Michael Darmady  
Laboratory, Queen Alexandra Hospital, Cosham, Portsmouth  
PO6 3LY, United Kingdom. ian.cree@port.ac.uk  
SOURCE: Current Opinion in Investigational Drugs, (2002) 3/4  
(641-647).  
Refs: 71  
ISSN: 1472-4472 CODEN: CIDREE  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
030 Pharmacology  
038 Adverse Reactions Titles  
029 Clinical Biochemistry  
022 Human Genetics  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT:

Chemosensitization strategies use the administration of one drug or agent to render cancer cells more susceptible to a second agent. Usually this involves enhanced drug metabolism, improvement of drug uptake or blockage of resistance mechanisms. Alteration of the susceptibility of cancer cells to apoptosis, the process of individual cell death by which many chemotherapeutic drugs act, shows particular promise for therapy in the future, and is the focus of this review. The dependence of cancer cells on non-neoplastic cells to form solid tumors allows anti-angiogenic therapy to be used in conjunction with chemotherapy to increase the therapeutic index. Chemosensitization strategies are set to become increasingly important in cancer therapy, allowing rational design of synergistic drug combinations at an earlier stage in drug development.

CONTROLLED TERM: Medical Descriptors:  
\*solid tumor: DT, drug therapy  
\*solid tumor: TH, therapy  
\*apoptosis  
\*cancer cell  
human  
clinical trial  
nonhuman  
drug metabolism  
drug uptake  
cell death

cancer combination chemotherapy  
leukemia cell  
chronic lymphatic leukemia: DT, drug therapy  
in vivo study  
oncogene neu  
drug potentiation  
cytotoxicity  
drug effect  
in vitro study  
drug targeting  
side effect: SI, side effect  
gene mutation  
enzyme inhibition  
gene therapy  
review  
Drug Descriptors:  
\*antineoplastic agent: DT, drug therapy  
\*antineoplastic agent: PD, pharmacology  
\*antineoplastic agent: IT, drug interaction  
\*antineoplastic agent: CB, drug combination  
\*antineoplastic agent: AE, adverse drug reaction  
\*antineoplastic agent: CT, clinical trial  
protein bcl 2: EC, endogenous compound  
antisense oligonucleotide: PD, pharmacology  
antisense oligonucleotide: IT, drug interaction  
protein bcl xl: EC, endogenous compound  
protein p53: EC, endogenous compound  
rituximab: PD, pharmacology  
cytotoxic agent: DT, drug therapy  
cytotoxic agent: PD, pharmacology  
cytotoxic agent: IT, drug interaction  
cytotoxic agent: CB, drug combination  
cytotoxic agent: AE, adverse drug reaction  
cytotoxic agent: CT, clinical trial  
growth factor receptor: EC, endogenous compound  
platinum derivative: PD, pharmacology  
platinum derivative: IT, drug interaction  
trastuzumab: PD, pharmacology  
trastuzumab: CB, drug combination  
trastuzumab: IT, drug interaction  
cyclooxygenase 2 inhibitor: PD, pharmacology  
cyclooxygenase 2 inhibitor: CB, drug combination  
cyclooxygenase 2 inhibitor: IT, drug interaction  
celecoxib: PD, pharmacology  
celecoxib: CB, drug combination  
celecoxib: IT, drug interaction  
epidermal growth factor receptor: EC, endogenous compound  
cetuximab: DT, drug therapy  
cetuximab: CT, clinical trial  
cetuximab: CB, drug combination  
cetuximab: IT, drug interaction  
cetuximab: PD, pharmacology  
protein tyrosine kinase inhibitor: PD, pharmacology  
protein tyrosine kinase inhibitor: DT, drug therapy  
protein tyrosine kinase inhibitor: CB, drug combination  
protein tyrosine kinase inhibitor: IT, drug interaction  
protein tyrosine kinase inhibitor: AE, adverse drug  
reaction  
protein tyrosine kinase inhibitor: CT, clinical trial  
erlotonib: PD, pharmacology  
zd 1839: PD, pharmacology  
gefitinib: PD, pharmacology  
paclitaxel: DT, drug therapy

paclitaxel: PD, pharmacology  
phosphatidylinositol 3 kinase: EC, endogenous compound  
cci 779: PD, pharmacology  
cci 779: DT, drug therapy  
cci 779: CB, drug combination  
cci 779: IT, drug interaction  
cci 779: AE, adverse drug reaction  
cci 779: CT, clinical trial  
protein kinase B: EC, endogenous compound  
cisplatin: DT, drug therapy  
cisplatin: PD, pharmacology  
cisplatin: IT, drug interaction  
cisplatin: CB, drug combination  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
irinotecan: IT, drug interaction  
**irinotecan: CB, drug combination**  
STAT protein: EC, endogenous compound  
imatinib: PD, pharmacology  
imatinib: DT, drug therapy  
Janus kinase: EC, endogenous compound  
proteasome inhibitor: PD, pharmacology  
protein kinase C inhibitor: PD, pharmacology  
unindexed drug  
unclassified drug  
osi 774  
[3 methyl 1 [[1 oxo 3 phenyl 2  
[(pyrazinylcarbonyl)amino]propyl]amino]butyl]boronic acid  
7 hydroxystaurosporine  
n benzoylstauosporine  
isis 3521  
ONYX 015

CAS REGISTRY NO.: (protein bcl 2) 219306-68-0; (protein bcl xl) 151033-38-4;  
(rituximab) 174722-31-7; (trastuzumab) 180288-69-1;  
(celecoxib) 169590-42-5; (cetuximab) 205923-56-4;  
(paclitaxel) 33069-62-4; (phosphatidylinositol 3 kinase)  
115926-52-8; (protein kinase B) 148640-14-6; (cisplatin)  
15663-27-1, 26035-31-4, 96081-74-2; (irinotecan)  
100286-90-6; (imatinib) 152459-95-5, 220127-57-1; (Janus  
kinase) 161384-16-3; ([3 methyl 1 [[1 oxo 3 phenyl 2  
[(pyrazinylcarbonyl)amino]propyl]amino]butyl]boronic acid)  
179324-69-7, 197730-97-5; (7 hydroxystaurosporine)  
112953-11-4; (n benzoylstauosporine) 120685-11-2; (isis  
3521) 151879-73-1

CHEMICAL NAME: (1) Herceptin; (2) C 225; (3) Osi 774; (4) Iressa; (5) Cci  
779; (6) Sti 571; (7) Ps 341; (8) Ucn 01; (9) Cgp 41251;  
(10) Isis 3521; (11) ONYX 015

COMPANY NAME: (1) Genentech; (2) Imclone; (3) Osi; (4) Astra Zeneca; (5)  
Wyeth; (7) Millennium Pharmaceuticals; (8) Kyowa Hakko  
Kogyo; (9) Novartis; (10) Isis; (11) Onyx; Idec; Pharmacia

L65 ANSWER 20 OF 26 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2002405308 EMBASE  
TITLE: 38th Annual Meeting of the American Society of Clinical  
Oncology.  
AUTHOR: Morse M.A.  
CORPORATE SOURCE: M.A. Morse, Department of Medicine, Duke University Medical  
Center, Durham, NC, United States. m.morse@cgct.duke.edu  
SOURCE: Expert Opinion on Emerging Drugs, (2002) 7/2 (335-338).  
ISSN: 1472-8214 CODEN: EOEDA3  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer  
030 Pharmacology  
036 Health Policy, Economics and Management  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
\*cancer research  
medical society  
chronic myeloid leukemia: DM, disease management  
chronic myeloid leukemia: DR, drug resistance  
chronic myeloid leukemia: DT, drug therapy  
nonhodgkin lymphoma: DT, drug therapy  
B cell lymphoma: DT, drug therapy  
digestive system cancer: DR, drug resistance  
digestive system cancer: DT, drug therapy  
colorectal cancer: DR, drug resistance  
colorectal cancer: DT, drug therapy  
kidney carcinoma: DT, drug therapy  
prostate cancer: DT, drug therapy  
lung non small cell cancer: DT, drug therapy  
gene mutation  
drug cytotoxicity  
drug potentiation  
cancer recurrence  
flu like syndrome: SI, side effect  
injection pain: SI, side effect  
acne: SI, side effect  
diarrhea: SI, side effect  
nausea: SI, side effect  
neutropenia: SI, side effect  
anorexia: SI, side effect  
weight reduction  
side effect: SI, side effect  
mucosa inflammation: SI, side effect  
rash: SI, side effect  
thromboembolism: SI, side effect  
cancer survival  
virus vector  
fever: SI, side effect  
headache: SI, side effect  
cancer immunotherapy  
bird disease  
dendritic cell  
anemia: CO, complication  
anemia: DT, drug therapy  
anemia: SI, side effect  
human  
nonhuman  
clinical trial  
conference paper  
Drug Descriptors:  
\*protein tyrosine kinase inhibitor: DT, drug therapy  
\*monoclonal antibody: DT, drug therapy  
imatinib: CT, clinical trial  
imatinib: CM, drug comparison  
imatinib: DT, drug therapy  
imatinib: PD, pharmacology  
recombinant alpha interferon: CT, clinical trial  
recombinant alpha interferon: CM, drug comparison  
recombinant alpha interferon: DT, drug therapy  
recombinant alpha interferon: PD, pharmacology

cytarabine: CT, clinical trial  
cytarabine: CM, drug comparison  
cytarabine: DT, drug therapy  
BCR ABL protein: EC, endogenous compound  
protein tyrosine kinase: EC, endogenous compound  
rituximab: CB, drug combination  
rituximab: IT, drug interaction  
rituximab: DT, drug therapy  
ibritumomab tiuxetan: DT, drug therapy  
tositumomab i 131: DT, drug therapy  
epratuzumab: CB, drug combination  
epratuzumab: DT, drug therapy  
interleukin 2: CB, drug combination  
interleukin 2: IT, drug interaction  
cancer vaccine: AE, adverse drug reaction  
cancer vaccine: CT, clinical trial  
cancer vaccine: DT, drug therapy  
prostate cancer vaccine: AE, adverse drug reaction  
prostate cancer vaccine: CT, clinical trial  
prostate cancer vaccine: DT, drug therapy  
apc 8015: AE, adverse drug reaction  
apc 8015: CT, clinical trial  
apc 8015: DT, drug therapy  
lung cancer vaccine: AE, adverse drug reaction  
lung cancer vaccine: CT, clinical trial  
lung cancer vaccine: DT, drug therapy  
keyhole limpet hemocyanin: DT, drug therapy  
granulocyte colony stimulating factor: AE, adverse drug reaction  
granulocyte colony stimulating factor: DO, drug dose  
granulocyte colony stimulating factor: DT, drug therapy  
cetuximab: AE, adverse drug reaction  
cetuximab: CB, drug combination  
cetuximab: DT, drug therapy  
irinotecan: AE, adverse drug reaction  
irinotecan: CB, drug combination  
irinotecan: IT, drug interaction  
irinotecan: DT, drug therapy  
celecoxib: CB, drug combination  
celecoxib: IT, drug interaction  
folinic acid: AE, adverse drug reaction  
folinic acid: CB, drug combination  
folinic acid: IT, drug interaction  
folinic acid: DT, drug therapy  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CB, drug combination  
fluorouracil: IT, drug interaction  
fluorouracil: DT, drug therapy  
bevacizumab: CT, clinical trial  
bevacizumab: DO, drug dose  
bevacizumab: DT, drug therapy  
diethylstilbestrol: DT, drug therapy  
gefitinib: CT, clinical trial  
gefitinib: DT, drug therapy  
recombinant erythropoietin: DT, drug therapy  
novel erythropoiesis stimulating protein: CT, clinical trial  
novel erythropoiesis stimulating protein: DT, drug therapy  
recombinant granulocyte colony stimulating factor: DT, drug therapy  
unindexed drug  
unclassified drug  
gvax

CAS REGISTRY NO.: provenge  
(imatinib) 152459-95-5, 220127-57-1; (cytarabine) 147-94-4,  
69-74-9; (protein tyrosine kinase) 80449-02-1; (rituximab)  
174722-31-7; (ibritumomab tiuxetan) 206181-63-7;  
(tositumomab i 131) 192391-48-3; (epratuzumab) 205923-57-5;  
(interleukin 2) 85898-30-2; (cetuximab) 205923-56-4;  
(irinotecan) 100286-90-6; (celecoxib) 169590-42-5; (folinic  
acid) 58-05-9, 68538-85-2; (fluorouracil) 51-21-8;  
(bevacizumab) 216974-75-3; (diethylstilbestrol) 30498-85-2,  
56-53-1; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7;  
(recombinant erythropoietin) 113427-24-0, 122312-54-3,  
130455-76-4; (recombinant granulocyte colony stimulating  
factor) 121181-53-1

CHEMICAL NAME: (1) Sti 571; (2) Gleevec; (3) Rituxan; (4) Bexxar; (5)  
Zevalin; (6) Imc c225; (7) Gvax; (8) Provenge; (9) Apc  
8015; (10) Neupogen; Iressa

COMPANY NAME: (2) Novartis; (3) Genentech; (4) Corixa; (5) Idec; (6)  
Imclone; (7) Cell Genesys; (9) Dendreon corp; (10) Amgen

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ACCESSION NUMBER: 2002227267 EMBASE

TITLE: Campath shows increased life expectancy for patients with  
advanced B-CLL.

SOURCE: Expert Review of Anticancer Therapy, (2002) 2/3 (241-247).  
ISSN: 1473-7140 CODEN: ERATBJ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Note

FILE SEGMENT: 016 Cancer  
025 Hematology  
030 Pharmacology  
036 Health Policy, Economics and Management  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
\*B cell leukemia: DT, drug therapy  
life expectancy  
cancer patient  
bone marrow metastasis: DT, drug therapy  
colorectal cancer: DT, drug therapy  
drug activity  
**antineoplastic activity**  
gastrointestinal symptom: SI, side effect  
fatigue: SI, side effect  
hand foot syndrome: SI, side effect  
rash: SI, side effect  
asthenia: SI, side effect  
neutropenia: SI, side effect  
mucosa inflammation: SI, side effect  
breast cancer: DT, drug therapy  
cancer survival  
recurrence risk  
cancer recurrence  
cancer staging  
stomatitis: SI, side effect  
lung cancer: DT, drug therapy  
lung cancer: RT, radiotherapy  
multimodality cancer therapy  
granulocytopenia: SI, side effect  
prostate cancer: DT, drug therapy  
edema: SI, side effect

rhinitis: SI, side effect  
headache: SI, side effect  
drug efficacy  
drug safety  
solid tumor: DT, drug therapy  
nonhodgkin lymphoma: DT, drug therapy  
esophagus cancer: DM, disease management  
esophagus cancer: DT, drug therapy  
human  
male  
female  
major clinical study  
clinical trial  
controlled study  
aged  
adult  
note  
Drug Descriptors:  
\*alemtuzumab: AN, drug analysis  
\*alemtuzumab: CB, drug combination  
\*alemtuzumab: DT, drug therapy  
\*alemtuzumab: PD, pharmacology  
fludarabine phosphate: AN, drug analysis  
fludarabine phosphate: CB, drug combination  
fludarabine phosphate: DT, drug therapy  
fludarabine phosphate: PD, pharmacology  
capecitabine: AE, adverse drug reaction  
capecitabine: AN, drug analysis  
capecitabine: CB, drug combination  
capecitabine: DO, drug dose  
capecitabine: DT, drug therapy  
capecitabine: PD, pharmacology  
capecitabine: PO, oral drug administration  
fluoropyrimidine: DT, drug therapy  
fluoropyrimidine: PD, pharmacology  
oxaliplatin: AN, drug analysis  
oxaliplatin: CB, drug combination  
oxaliplatin: DT, drug therapy  
oxaliplatin: PD, pharmacology  
oxaliplatin: IV, intravenous drug administration  
irinotecan: AE, adverse drug reaction  
irinotecan: CT, clinical trial  
irinotecan: AN, drug analysis  
    **irinotecan: CB, drug combination**  
irinotecan: DO, drug dose  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
irinotecan: IV, intravenous drug administration  
celecoxib: AE, adverse drug reaction  
celecoxib: AN, drug analysis  
    **celecoxib: CB, drug combination**  
celecoxib: DT, drug therapy  
celecoxib: PD, pharmacology  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: AN, drug analysis  
fluorouracil: CB, drug combination  
fluorouracil: CM, drug comparison  
fluorouracil: DT, drug therapy  
fluorouracil: PD, pharmacology  
folinic acid: AE, adverse drug reaction  
folinic acid: CT, clinical trial  
folinic acid: AN, drug analysis

folinic acid: CB, drug combination  
folinic acid: DT, drug therapy  
folinic acid: PD, pharmacology  
cetuximab: AE, adverse drug reaction  
cetuximab: CT, clinical trial  
cetuximab: AN, drug analysis  
cetuximab: CB, drug combination  
cetuximab: DT, drug therapy  
cetuximab: PD, pharmacology  
docetaxel: CT, clinical trial  
docetaxel: AN, drug analysis  
docetaxel: CB, drug combination  
docetaxel: CM, drug comparison  
docetaxel: DT, drug therapy  
docetaxel: PD, pharmacology  
doxorubicin: CT, clinical trial  
doxorubicin: AN, drug analysis  
doxorubicin: CB, drug combination  
doxorubicin: CM, drug comparison  
doxorubicin: DT, drug therapy  
doxorubicin: PD, pharmacology  
cyclophosphamide: CT, clinical trial  
cyclophosphamide: AN, drug analysis  
cyclophosphamide: CB, drug combination  
cyclophosphamide: CM, drug comparison  
cyclophosphamide: DT, drug therapy  
cyclophosphamide: PD, pharmacology  
paclitaxel: AE, adverse drug reaction  
paclitaxel: CT, clinical trial  
paclitaxel: AN, drug analysis  
paclitaxel: CB, drug combination  
paclitaxel: CM, drug comparison  
paclitaxel: DO, drug dose  
paclitaxel: DT, drug therapy  
paclitaxel: PD, pharmacology  
carboplatin: AE, adverse drug reaction  
carboplatin: CT, clinical trial  
carboplatin: AN, drug analysis  
carboplatin: CB, drug combination  
carboplatin: CM, drug comparison  
carboplatin: DT, drug therapy  
carboplatin: PD, pharmacology  
squalamine: CT, clinical trial  
squalamine: AN, drug analysis  
squalamine: CB, drug combination  
squalamine: CM, drug comparison  
squalamine: DO, drug dose  
squalamine: DT, drug therapy  
squalamine: PD, pharmacology  
polyglutamate paclitaxel: CT, clinical trial  
polyglutamate paclitaxel: AN, drug analysis  
polyglutamate paclitaxel: DT, drug therapy  
polyglutamate paclitaxel: PD, pharmacology  
paclitaxel derivative: CT, clinical trial  
paclitaxel derivative: AN, drug analysis  
paclitaxel derivative: DT, drug therapy  
paclitaxel derivative: PD, pharmacology  
atrasentan: AE, adverse drug reaction  
atrasentan: CT, clinical trial  
atrasentan: AN, drug analysis  
atrasentan: DO, drug dose  
atrasentan: DT, drug therapy  
atrasentan: PD, pharmacology

atrasentan: PO, oral drug administration  
placebo  
gvax: CT, clinical trial  
gvax: AN, drug analysis  
gvax: DO, drug dose  
gvax: DT, drug therapy  
gvax: PD, pharmacology  
gvax: DL, intradermal drug administration  
cancer vaccine: CT, clinical trial  
cancer vaccine: AN, drug analysis  
cancer vaccine: DO, drug dose  
cancer vaccine: DT, drug therapy  
cancer vaccine: PD, pharmacology  
cancer vaccine: DL, intradermal drug administration  
apolizumab: CT, clinical trial  
apolizumab: AN, drug analysis  
apolizumab: DO, drug dose  
apolizumab: DT, drug therapy  
apolizumab: PK, pharmacokinetics  
apolizumab: PD, pharmacology  
apolizumab: IV, intravenous drug administration  
antibody: CT, clinical trial  
antibody: AN, drug analysis  
antibody: DO, drug dose  
antibody: DT, drug therapy  
antibody: PK, pharmacokinetics  
antibody: PD, pharmacology  
antibody: IV, intravenous drug administration  
rituximab: CT, clinical trial  
rituximab: AN, drug analysis  
rituximab: CB, drug combination  
rituximab: DT, drug therapy  
rituximab: PD, pharmacology  
bryostatin 1: CT, clinical trial  
bryostatin 1: AN, drug analysis  
bryostatin 1: CB, drug combination  
bryostatin 1: DV, drug development  
bryostatin 1: DT, drug therapy  
bryostatin 1: PE, pharmacoeconomics  
bryostatin 1: PD, pharmacology  
lymphorad: CT, clinical trial  
lymphorad: AN, drug analysis  
lymphorad: DT, drug therapy  
lymphorad: PD, pharmacology  
interleukin 4: CT, clinical trial  
interleukin 4: AN, drug analysis  
interleukin 4: CB, drug combination  
interleukin 4: DT, drug therapy  
interleukin 4: PD, pharmacology  
iodine 131: CT, clinical trial  
iodine 131: AN, drug analysis  
iodine 131: CB, drug combination  
iodine 131: DT, drug therapy  
iodine 131: PD, pharmacology  
unindexed drug  
unclassified drug  
erbitux  
xyotax  
abt 627  
remitogen

CAS REGISTRY NO.: (alemtuzumab) 216503-57-0; (fludarabine phosphate)  
75607-67-9; (capecitabine) 154361-50-9; (fluoropyrimidine)  
675-21-8; (oxaliplatin) 61825-94-3; (irinotecan)

100286-90-6; (celecoxib) 169590-42-5; (fluorouracil)  
51-21-8; (folinic acid) 58-05-9, 68538-85-2; (cetuximab)  
205923-56-4; (docetaxel) 114977-28-5; (doxorubicin)  
23214-92-8, 25316-40-9; (cyclophosphamide) 50-18-0;  
(paclitaxel) 33069-62-4; (carboplatin) 41575-94-4;  
(squalamine) 148717-90-2, 160022-48-0; (atrasentan)  
197448-99-0; (rituximab) 174722-31-7; (bryostatin 1)  
83314-01-6; (iodine 131) 10043-66-0, 15124-39-7; (abt 627)  
173937-91-2

CHEMICAL NAME: (1) Campath; (2) Mabcampath; (3) Xeloda; (4) Erbitux; (5)  
Erbitux; (6) Taxotere; (7) Xyotax; (8) Abt 627; (9) Gvax;  
(10) Remitogen; Fludara; Eloxatin; Camptosar; Celebrex;  
Cytosan; Adriamycin; Taxol; Paraplatin

COMPANY NAME: (1) Berlex (United States); (2) Schering AG (United  
Kingdom); (3) Hoffmann La Roche; (4) Imclone; (5) Bristol  
Myers Squibb; (6) Aventis; (7) Cell Therapeutics; (8)  
Abbott; (9) Cell Genesys; (10) Protein Design; Genaera;  
Orphan

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ACCESSION NUMBER: 2002391205 EMBASE

TITLE: [New development in oncology. Report of the first North  
German Cytostatics Workshop in Ravensburg].  
NEUE ENTWICKLUNGEN IN DER ONKOLOGIE: BERICHT VOM I. NZW-SUD  
IN RAVENSBURG.

SOURCE: Deutsche Apotheker Zeitung, (24 Oct 2002) 142/43 (46-53).  
ISSN: 0011-9857 CODEN: DAZE2

COUNTRY: Germany

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: German

CONTROLLED TERM: Medical Descriptors:  
\*cancer research  
\*cancer chemotherapy  
medical society  
Germany  
oncology  
prognosis  
preoperative care  
angiogenesis  
disease marker  
cancer hormone therapy  
tumor classification  
premenopause  
postmenopause  
breast carcinoma: DT, drug therapy  
colon carcinoma: DT, drug therapy  
neutropenia: SI, side effect  
lung carcinoma: DT, drug therapy  
human  
clinical trial  
conference paper  
Drug Descriptors:  
taxane derivative: DT, drug therapy  
trastuzumab: DT, drug therapy  
tamoxifen: CB, drug combination  
tamoxifen: DT, drug therapy  
gonadorelin agonist: CB, drug combination  
gonadorelin agonist: DT, drug therapy

goserelin: CB, drug combination  
goserelin: DT, drug therapy  
anastrozole: CB, drug combination  
anastrozole: DT, drug therapy  
letrozole: DT, drug therapy  
paclitaxel: DT, drug therapy  
fluorouracil derivative: DT, drug therapy  
fluorouracil derivative: PO, oral drug administration  
doxorubicin: DT, drug therapy  
folinic acid: CT, clinical trial  
folinic acid: CB, drug combination  
folinic acid: DT, drug therapy  
fluorouracil: AE, adverse drug reaction  
fluorouracil: CT, clinical trial  
fluorouracil: CM, drug comparison  
fluorouracil: DT, drug therapy  
fluorouracil: IV, intravenous drug administration  
irinotecan: AE, adverse drug reaction  
irinotecan: CB, drug combination  
irinotecan: DT, drug therapy  
oxaliplatin: AE, adverse drug reaction  
oxaliplatin: CB, drug combination  
oxaliplatin: DT, drug therapy  
capecitabine: CB, drug combination  
capecitabine: DT, drug therapy  
tegafur: CB, drug combination  
tegafur: DT, drug therapy  
UFT: CB, drug combination  
UFT: DT, drug therapy  
cyclooxygenase 2 inhibitor: CB, drug combination  
epidermal growth factor receptor  
vasculotropin inhibitor  
bevacizumab: DT, drug therapy  
cetuximab  
celecoxib: CT, clinical trial  
celecoxib: CB, drug combination  
protein tyrosine kinase inhibitor: DT, drug therapy  
carboplatin: CB, drug combination  
carboplatin: DT, drug therapy  
cisplatin: CB, drug combination  
cisplatin: DT, drug therapy  
docetaxel: CB, drug combination  
docetaxel: DT, drug therapy  
protein kinase C inhibitor: DT, drug therapy  
granulocyte macrophage colony stimulating factor  
unindexed drug

CAS REGISTRY NO.: (trastuzumab) 180288-69-1; (tamoxifen) 10540-29-1;  
(goserelin) 65807-02-5; (anastrozole) 120511-73-1;  
(letrozole) 112809-51-5; (paclitaxel) 33069-62-4;  
(doxorubicin) 23214-92-8, 25316-40-9; (folinic acid)  
58-05-9, 68538-85-2; (fluorouracil) 51-21-8; (irinotecan)  
100286-90-6; (oxaliplatin) 61825-94-3; (capecitabine)  
154361-50-9; (tegafur) 17902-23-7; (UFT) 74578-38-4;  
(bevacizumab) 216974-75-3; (cetuximab) 205923-56-4;  
(celecoxib) 169590-42-5; (carboplatin) 41575-94-4;  
(cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (docetaxel)  
114977-28-5  
CHEMICAL NAME: Herceptin; Zoladex; Arimidex; Femara; Xeloda; UFT;  
Eloxatin; Campto; Avastin

L65 ANSWER 23 OF 26 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 2002298390 EMBASE

TITLE: Highlights from: 38th Annual Meeting of the American Society of clinical oncology.

AUTHOR: DeGrendele H.; Belani C.P.; Jain V.K.

SOURCE: Clinical Lung Cancer, (2002) 4/1 (16-20).  
Refs: 20  
ISSN: 1525-7304 CODEN: CLCLCA

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
\*lung non small cell cancer: DI, diagnosis  
\*lung non small cell cancer: DT, drug therapy  
\*lung small cell cancer: DI, diagnosis  
\*lung small cell cancer: DT, drug therapy  
cancer combination chemotherapy  
advanced cancer: DI, diagnosis  
advanced cancer: DT, drug therapy  
patient care  
cancer patient  
cancer survival  
cancer mortality  
treatment outcome  
quality of life  
drug efficacy  
cancer diagnosis  
blood toxicity: SI, side effect  
nausea: SI, side effect  
vomiting: SI, side effect  
febrile neutropenia: SI, side effect  
dose response  
cancer growth  
drug tolerability  
prognosis  
human  
male  
female  
clinical trial  
controlled study  
conference paper  
Drug Descriptors:  
\*antineoplastic agent: AE, adverse drug reaction  
\*antineoplastic agent: CT, clinical trial  
\*antineoplastic agent: CB, drug combination  
\*antineoplastic agent: CM, drug comparison  
\*antineoplastic agent: DO, drug dose  
\*antineoplastic agent: DT, drug therapy  
\*antineoplastic agent: PD, pharmacology  
\*antineoplastic agent: PO, oral drug administration  
cisplatin: AE, adverse drug reaction  
cisplatin: CT, clinical trial  
cisplatin: CB, drug combination  
cisplatin: CM, drug comparison  
cisplatin: DO, drug dose  
cisplatin: DT, drug therapy  
cisplatin: PD, pharmacology  
cisplatin: PO, oral drug administration  
vindesine: AE, adverse drug reaction

vindesine: CB, drug combination  
vindesine: CM, drug comparison  
vindesine: DT, drug therapy  
vindesine: PD, pharmacology  
mitomycin: AE, adverse drug reaction  
mitomycin: CB, drug combination  
mitomycin: CM, drug comparison  
mitomycin: DT, drug therapy  
mitomycin: PD, pharmacology  
ifosfamide: AE, adverse drug reaction  
ifosfamide: CB, drug combination  
ifosfamide: CM, drug comparison  
ifosfamide: DT, drug therapy  
ifosfamide: PD, pharmacology  
vinblastine: AE, adverse drug reaction  
vinblastine: CB, drug combination  
vinblastine: CM, drug comparison  
vinblastine: DT, drug therapy  
vinblastine: PD, pharmacology  
navelbine: AE, adverse drug reaction  
navelbine: CB, drug combination  
navelbine: CM, drug comparison  
navelbine: DT, drug therapy  
navelbine: PD, pharmacology  
paclitaxel: AE, adverse drug reaction  
paclitaxel: CT, clinical trial  
paclitaxel: CB, drug combination  
paclitaxel: CM, drug comparison  
paclitaxel: DO, drug dose  
paclitaxel: DT, drug therapy  
paclitaxel: PD, pharmacology  
etoposide: AE, adverse drug reaction  
etoposide: CT, clinical trial  
etoposide: CB, drug combination  
etoposide: CM, drug comparison  
etoposide: DO, drug dose  
etoposide: DT, drug therapy  
etoposide: PD, pharmacology  
recombinant granulocyte colony stimulating factor: AE, adverse drug reaction  
recombinant granulocyte colony stimulating factor: CB, drug combination  
recombinant granulocyte colony stimulating factor: CM, drug comparison  
recombinant granulocyte colony stimulating factor: DO, drug dose  
recombinant granulocyte colony stimulating factor: DT, drug therapy  
recombinant granulocyte colony stimulating factor: PD, pharmacology  
irinotecan: AE, adverse drug reaction  
irinotecan: CT, clinical trial  
irinotecan: CB, drug combination  
irinotecan: CM, drug comparison  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
imatinib: AE, adverse drug reaction  
imatinib: CT, clinical trial  
imatinib: DT, drug therapy  
imatinib: PD, pharmacology  
protein kinase inhibitor: AE, adverse drug reaction  
protein kinase inhibitor: CT, clinical trial  
protein kinase inhibitor: DT, drug therapy

protein kinase inhibitor: PD, pharmacology  
 BCR ABL protein: EC, endogenous compound  
 protein tyrosine kinase: EC, endogenous compound  
 platelet derived growth factor receptor: EC, endogenous compound

stem cell factor: EC, endogenous compound  
 stem cell factor receptor: EC, endogenous compound  
 celecoxib: AE, adverse drug reaction

**celecoxib: CB, drug combination**

celecoxib: DT, drug therapy  
 celecoxib: PD, pharmacology  
 prostaglandin synthase: EC, endogenous compound  
 cyclooxygenase 2: EC, endogenous compound  
 cyclooxygenase 2 inhibitor: EC, endogenous compound  
 prostaglandin E2: EC, endogenous compound  
 vasculotropin: EC, endogenous compound  
 matrix metalloproteinase: EC, endogenous compound  
 nonsteroid antiinflammatory agent: DT, drug therapy  
 nonsteroid antiinflammatory agent: PD, pharmacology  
 taxane derivative: DT, drug therapy  
 taxane derivative: PD, pharmacology

CAS REGISTRY NO.: (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (vindesine) 53643-48-4; (mitomycin) 1404-00-8; (ifosfamide) 3778-73-2; (vinblastine) 865-21-4; (navelbine) 71486-22-1; (paclitaxel) 33069-62-4; (etoposide) 33419-42-0; (recombinant granulocyte colony stimulating factor) 121181-53-1; (irinotecan) 100286-90-6; (imatinib) 152459-95-5, 220127-57-1; (protein tyrosine kinase) 80449-02-1; (celecoxib) 169590-42-5; (prostaglandin synthase) 39391-18-9, 59763-19-8, 9055-65-6; (prostaglandin E2) 363-24-6; (vasculotropin) 127464-60-2

CHEMICAL NAME: Filgrastim; Gleevec

L65 ANSWER 24 OF 26 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 2003019359 EMBASE  
 TITLE: Irinotecan in non-small-cell lung cancer: Status of ongoing trials.

AUTHOR: Socinski M.A.

CORPORATE SOURCE: Dr. M.A. Socinski, The Mltidisc. Thoracic Oncol. Prog.,  
 Lineberger Comp. Cancer Center, University of North  
 Carolina, Chapel Hill, NC, United States.  
 socinski@med.unc.edu

SOURCE: Clinical Lung Cancer, (2002) 4/SUPPL. 1 (S15-S20).  
 Refs: 55

ISSN: 1525-7304 CODEN: CLCLCA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:**

Irinotecan possesses significant single-agent activity in non-small-cell lung cancer (NSCLC) and is active in combination with either cisplatin or carboplatin. Two phase III trials completed in Japan have suggested that the combination of irinotecan/cisplatin yields superior survival rates in stage IV NSCLC patients compared to vindesine/cisplatin. The principal toxicities of the irinotecan/cisplatin regimen are neutropenia and diarrhea. This regimen is currently being tested in Japan against regimens commonly used in the United

States, such as cisplatin/gemcitabine, cisplatin/vinorelbine, and carboplatin/paclitaxel. These studies include evaluation of monthly as well as weekly schedules of cisplatin in combination with irinotecan as well as a triplet regimen of irinotecan/carboplatin/paclitaxel. Ongoing trials are evaluating these regimens as well as irinotecan/carboplatin and several nonplatinum-based irinotecan-containing doublets in both the first- and second-line treatment of advanced NSCLC. Several ongoing trials are attempting to integrate irinotecan with thoracic radiation therapy in stage III NSCLC. These trials are using irinotecan-containing regimens as induction and concurrent therapy with thoracic radiation therapy. Irinotecan is also being evaluated in the preoperative setting in early-stage resectable NSCLC. Many of these trials are also incorporating celecoxib, a potent inhibitor of the cyclooxygenase-2 pathway, in combination with irinotecan-containing regimens in both advanced as well as early-stage NSCLC. Future trials should focus on the integration of the new targeted agents in combination with irinotecan-containing regimens in all stages of NSCLC.

CONTROLLED TERM: Medical Descriptors:  
 \*lung non small cell cancer: DT, drug therapy  
 \*lung non small cell cancer: RT, radiotherapy  
 \*lung non small cell cancer: SU, surgery  
     **antineoplastic activity**  
     **cancer combination chemotherapy**  
     cancer survival  
     cancer staging  
     neutropenia: SI, side effect  
     diarrhea: SI, side effect  
     Japan  
     United States  
     drug dose regimen  
     cancer radiotherapy  
     preoperative care  
     lung resection  
     drug targeting  
     drug metabolism  
     thrombocytopenia: SI, side effect  
     anemia: SI, side effect  
     nausea and vomiting: SI, side effect  
     area under the curve  
     febrile neutropenia: DT, drug therapy  
     febrile neutropenia: PC, prevention  
     febrile neutropenia: SI, side effect  
     asthenia: SI, side effect  
     human  
     clinical trial  
     meta analysis  
     controlled study  
     article  
 Drug Descriptors:  
 \*irinotecan: AE, adverse drug reaction  
 \*irinotecan: CT, clinical trial  
     **\*irinotecan: CB, drug combination**  
 \*irinotecan: CM, drug comparison  
 \*irinotecan: DO, drug dose  
 \*irinotecan: DT, drug therapy  
 \*irinotecan: PK, pharmacokinetics  
 \*irinotecan: PD, pharmacology  
 cisplatin: AE, adverse drug reaction  
 cisplatin: CT, clinical trial  
 cisplatin: CB, drug combination  
 cisplatin: CM, drug comparison  
 cisplatin: DO, drug dose  
 cisplatin: DT, drug therapy

cisplatin: PD, pharmacology  
carboplatin: AE, adverse drug reaction  
carboplatin: CT, clinical trial  
carboplatin: CB, drug combination  
carboplatin: CM, drug comparison  
carboplatin: DO, drug dose  
carboplatin: DT, drug therapy  
carboplatin: PK, pharmacokinetics  
carboplatin: PD, pharmacology  
vindesine: AE, adverse drug reaction  
vindesine: CT, clinical trial  
vindesine: CB, drug combination  
vindesine: CM, drug comparison  
vindesine: DO, drug dose  
vindesine: DT, drug therapy  
vindesine: PD, pharmacology  
gemcitabine: AE, adverse drug reaction  
gemcitabine: CT, clinical trial  
gemcitabine: CB, drug combination  
gemcitabine: CM, drug comparison  
gemcitabine: DO, drug dose  
gemcitabine: DT, drug therapy  
gemcitabine: PD, pharmacology  
navelbine: AE, adverse drug reaction  
navelbine: CT, clinical trial  
navelbine: CB, drug combination  
navelbine: CM, drug comparison  
navelbine: DO, drug dose  
navelbine: DT, drug therapy  
navelbine: PD, pharmacology  
paclitaxel: AE, adverse drug reaction  
paclitaxel: CT, clinical trial  
paclitaxel: CB, drug combination  
paclitaxel: CM, drug comparison  
paclitaxel: DO, drug dose  
paclitaxel: DT, drug therapy  
paclitaxel: PD, pharmacology  
celecoxib: CT, clinical trial  
**celecoxib: CB, drug combination**  
celecoxib: CM, drug comparison  
celecoxib: DO, drug dose  
celecoxib: IT, drug interaction  
celecoxib: DT, drug therapy  
celecoxib: PD, pharmacology  
celecoxib: PO, oral drug administration  
**cyclooxygenase 2 inhibitor: CB, drug combination**  
cyclooxygenase 2 inhibitor: DT, drug therapy  
cyclooxygenase 2 inhibitor: PD, pharmacology  
etoposide: CT, clinical trial  
etoposide: CB, drug combination  
etoposide: CM, drug comparison  
etoposide: IT, drug interaction  
etoposide: DT, drug therapy  
etoposide: PD, pharmacology  
Vinca alkaloid: CB, drug combination  
Vinca alkaloid: CM, drug comparison  
Vinca alkaloid: DT, drug therapy  
Vinca alkaloid: PD, pharmacology  
mitomycin: CB, drug combination  
mitomycin: CM, drug comparison  
mitomycin: DT, drug therapy  
mitomycin: PD, pharmacology  
7 ethyl 10 hydroxycamptothecin: AE, adverse drug reaction

7 ethyl 10 hydroxycamptothecin: CT, clinical trial  
7 ethyl 10 hydroxycamptothecin: CB, drug combination  
7 ethyl 10 hydroxycamptothecin: CM, drug comparison  
7 ethyl 10 hydroxycamptothecin: DO, drug dose  
7 ethyl 10 hydroxycamptothecin: IT, drug interaction  
7 ethyl 10 hydroxycamptothecin: DT, drug therapy  
7 ethyl 10 hydroxycamptothecin: PK, pharmacokinetics  
7 ethyl 10 hydroxycamptothecin: PD, pharmacology  
platinum derivative: AE, adverse drug reaction  
platinum derivative: CT, clinical trial  
platinum derivative: CB, drug combination  
platinum derivative: CM, drug comparison  
platinum derivative: DO, drug dose  
platinum derivative: IT, drug interaction  
platinum derivative: DT, drug therapy  
platinum derivative: PD, pharmacology  
DNA topoisomerase inhibitor: AE, adverse drug reaction  
DNA topoisomerase inhibitor: CT, clinical trial  
DNA topoisomerase inhibitor: CB, drug combination  
DNA topoisomerase inhibitor: CM, drug comparison  
DNA topoisomerase inhibitor: DO, drug dose  
DNA topoisomerase inhibitor: IT, drug interaction  
DNA topoisomerase inhibitor: DT, drug therapy  
DNA topoisomerase inhibitor: PK, pharmacokinetics  
DNA topoisomerase inhibitor: PD, pharmacology  
antibody: DT, drug therapy  
ifosfamide: AE, adverse drug reaction  
ifosfamide: CT, clinical trial  
ifosfamide: CB, drug combination  
ifosfamide: CM, drug comparison  
ifosfamide: DT, drug therapy  
ifosfamide: PD, pharmacology  
docetaxel: AE, adverse drug reaction  
docetaxel: CT, clinical trial  
docetaxel: CB, drug combination  
docetaxel: CM, drug comparison  
docetaxel: IT, drug interaction  
docetaxel: DT, drug therapy  
docetaxel: PD, pharmacology  
thalidomide: CT, clinical trial  
thalidomide: CB, drug combination  
thalidomide: CM, drug comparison  
thalidomide: DT, drug therapy  
thalidomide: PD, pharmacology  
temozolomide: CT, clinical trial  
temozolomide: CB, drug combination  
temozolomide: CM, drug comparison  
temozolomide: DT, drug therapy  
temozolomide: PD, pharmacology  
epidermal growth factor: DT, drug therapy  
receptor blocking agent: CB, drug combination  
receptor blocking agent: PD, pharmacology  
angiogenesis inhibitor: CB, drug combination  
angiogenesis inhibitor: PD, pharmacology  
antisense oligonucleotide: CB, drug combination  
antisense oligonucleotide: PD, pharmacology  
(irinotecan) 100286-90-6; (cisplatin) 15663-27-1,  
26035-31-4, 96081-74-2; (carboplatin) 41575-94-4;  
(vindesine) 53643-48-4; (gemcitabine) 103882-84-4;  
(navelbine) 71486-22-1; (paclitaxel) 33069-62-4;  
(celecoxib) 169590-42-5; (etoposide) 33419-42-0;  
(mitomycin) 1404-00-8; (7 ethyl 10 hydroxycamptothecin)  
86639-52-3; (ifosfamide) 3778-73-2; (docetaxel)

CAS REGISTRY NO.:

CHEMICAL NAME: 114977-28-5; (thalidomide) 50-35-1; (temozolomide)  
85622-93-1; (epidermal growth factor) 62229-50-9  
Sn 38; Vp 16

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ACCESSION NUMBER: 2002344439 EMBASE  
TITLE: [Onkologie: Preface].  
VORWORT.  
AUTHOR: Schmoll H.-J.  
SOURCE: Onkologie, (2002) 25/SUPPL. 3 (V-VI).  
ISSN: 0378-584X CODEN: ONKOD2  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; Editorial  
FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
048 Gastroenterology  
LANGUAGE: German

CONTROLLED TERM: Medical Descriptors:  
\*colorectal cancer: DT, drug therapy  
\*colorectal cancer: SU, surgery  
cancer surgery  
cancer palliative therapy  
cancer regression  
prognosis  
adjuvant chemotherapy  
enzyme inhibition  
cell proliferation  
drug infusion  
monotherapy  
cancer combination chemotherapy  
human  
editorial  
Drug Descriptors:  
fluorouracil: CB, drug combination  
fluorouracil: DT, drug therapy  
fluorouracil: PD, pharmacology  
oxaliplatin: CB, drug combination  
oxaliplatin: DT, drug therapy  
oxaliplatin: PD, pharmacology  
irinotecan: CB, drug combination  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
capecitabine: CB, drug combination  
capecitabine: DT, drug therapy  
capecitabine: PD, pharmacology  
UFT: DT, drug therapy  
UFT: PD, pharmacology  
cetuximab: DT, drug therapy  
cetuximab: PD, pharmacology  
epidermal growth factor receptor: EC, endogenous compound  
protein tyrosine kinase inhibitor: DT, drug therapy  
protein tyrosine kinase inhibitor: PD, pharmacology  
cyclooxygenase 2 inhibitor: CB, drug combination  
cyclooxygenase 2 inhibitor: DT, drug therapy  
cyclooxygenase 2 inhibitor: PD, pharmacology  
cyclooxygenase 2 inhibitor: PO, oral drug administration  
CAS REGISTRY NO.: (fluorouracil) 51-21-8; (oxaliplatin) 61825-94-3;  
(irinotecan) 100286-90-6; (capecitabine) 154361-50-9; (UFT)  
74578-38-4; (cetuximab) 205923-56-4  
CHEMICAL NAME: Eloxatin

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ACCESSION NUMBER: 2001290717 EMBASE  
TITLE: [What kind of chemotherapy for metastatic pancreatic adenocarcinomas?].  
LES ADENOCARCINOMES PANCREATIQUES METASTATIQUES: QUELLE CHIMIOTHERAPIE?  
AUTHOR: Legoux J.-L.; Smith D.  
CORPORATE SOURCE: J.-L. Legoux, Service d'Hepato-Gastroenterologie, Hopital du Haut-Leveque, CHU de Bordeaux, 5, avenue de Magellan, 33604 Pessac, France  
SOURCE: Hepato-Gastro, (2001) 8/4 (273-277).  
Refs: 33  
ISSN: 1253-7020 CODEN: HEGAF6  
COUNTRY: France  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
048 Gastroenterology  
LANGUAGE: French  
CONTROLLED TERM: Medical Descriptors:  
\*pancreas adenocarcinoma: DT, drug therapy  
\*metastasis: CO, complication  
\*metastasis: DT, drug therapy  
\*cancer chemotherapy  
drug choice  
cancer combination chemotherapy  
drug efficacy  
cancer survival  
human  
clinical trial  
short survey  
Drug Descriptors:  
\*fluorouracil: CT, clinical trial  
\*fluorouracil: CB, drug combination  
\*fluorouracil: DT, drug therapy  
\*fluorouracil: PD, pharmacology  
\*cisplatin: CT, clinical trial  
\*cisplatin: CB, drug combination  
\*cisplatin: DT, drug therapy  
\*cisplatin: PD, pharmacology  
\*gemcitabine: CT, clinical trial  
\*gemcitabine: CB, drug combination  
\*gemcitabine: DT, drug therapy  
\*gemcitabine: PD, pharmacology  
cyclophosphamide: CT, clinical trial  
cyclophosphamide: CB, drug combination  
cyclophosphamide: DT, drug therapy  
cyclophosphamide: PD, pharmacology  
methotrexate: CT, clinical trial  
methotrexate: CB, drug combination  
methotrexate: DT, drug therapy  
methotrexate: PD, pharmacology  
mitomycin C: CT, clinical trial  
mitomycin C: CB, drug combination  
mitomycin C: DT, drug therapy  
mitomycin C: PD, pharmacology  
doxorubicin: CT, clinical trial  
doxorubicin: CB, drug combination  
doxorubicin: DT, drug therapy  
doxorubicin: PD, pharmacology  
folic acid: CT, clinical trial

folic acid: CB, drug combination  
folic acid: DT, drug therapy  
folic acid: PD, pharmacology  
etoposide: CT, clinical trial  
etoposide: CB, drug combination  
etoposide: DT, drug therapy  
etoposide: PD, pharmacology  
oxaliplatin: CT, clinical trial  
oxaliplatin: CB, drug combination  
oxaliplatin: DT, drug therapy  
oxaliplatin: PD, pharmacology  
epirubicin: CT, clinical trial  
epirubicin: CB, drug combination  
epirubicin: DT, drug therapy  
epirubicin: PD, pharmacology  
irinotecan: CT, clinical trial  
**irinotecan: CB, drug combination**  
irinotecan: DT, drug therapy  
irinotecan: PD, pharmacology  
taxotere: CT, clinical trial  
taxotere: CB, drug combination  
taxotere: DT, drug therapy  
taxotere: PD, pharmacology  
interferon: CT, clinical trial  
interferon: CB, drug combination  
interferon: DT, drug therapy  
taxane derivative: CT, clinical trial  
taxane derivative: CB, drug combination  
taxane derivative: DT, drug therapy  
raltitrexed: CT, clinical trial  
raltitrexed: CB, drug combination  
raltitrexed: DT, drug therapy  
6 hydroxymethylacylfulvene: CT, clinical trial  
6 hydroxymethylacylfulvene: CB, drug combination  
6 hydroxymethylacylfulvene: DT, drug therapy  
rubitecan: CT, clinical trial  
rubitecan: CB, drug combination  
rubitecan: DT, drug therapy  
cyclooxygenase 2 inhibitor: CT, clinical trial  
**cyclooxygenase 2 inhibitor: CB, drug combination**  
cyclooxygenase 2 inhibitor: DT, drug therapy  
flutamide: CT, clinical trial  
flutamide: CB, drug combination  
flutamide: DT, drug therapy  
UFT: CT, clinical trial  
UFT: CB, drug combination  
UFT: DT, drug therapy  
capecitabine: CT, clinical trial  
capecitabine: CB, drug combination  
capecitabine: DT, drug therapy  
4 n acetyldinaline: CT, clinical trial  
4 n acetyldinaline: CB, drug combination  
4 n acetyldinaline: DT, drug therapy  
CAS REGISTRY NO.: (fluorouracil) 51-21-8; (cisplatin) 15663-27-1, 26035-31-4,  
96081-74-2; (gemcitabine) 103882-84-4; (cyclophosphamide)  
50-18-0; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5;  
(mitomycin C) 50-07-7, 74349-48-7; (doxorubicin)  
23214-92-8, 25316-40-9; (folic acid) 59-30-3, 6484-89-5;  
(etoposide) 33419-42-0; (oxaliplatin) 61825-94-3;  
(epirubicin) 56390-09-1, 56420-45-2; (irinotecan)  
100286-90-6; (taxotere) 114977-28-5; (raltitrexed)  
112887-68-0; (6 hydroxymethylacylfulvene) 158440-71-2;  
(rubitecan) 91421-42-0; (flutamide) 13311-84-7; (UFT)

CHEMICAL NAME: 74578-38-4; (capecitabine) 154361-50-9; (4 n  
acetyldinaline) 112522-64-2  
Cpt 11; Mgi 114; Ci 994

FILE 'HOME' ENTERED AT 09:56:19 ON 22 OCT 2003